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ANNALS OF INTERNAL MEDICINE

VOLUME 10

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THE TREATMENT OF PNEUMONIA *

By RUFUS COLE, M.D., *New York, N. Y.*

THIRTY years ago Dr. Osler wrote, "Pneumonia is a self-limited disease, which can neither be aborted nor cut short by any means at our command." When I went to the Rockefeller Institute shortly afterwards, I said to myself, "Here, at least, is a wide open field. This is the most serious acute infectious disease with which physicians have to deal. Is it possible that nothing can be done to decrease the frightful mortality due to this malady? At any rate, we can attempt to obey St. Paul's injunction, 'Prove all things, hold fast that which is good.' " From that time to this, my associates and I have tested many new things, and while we have tried to hold fast to that which is good, we may have failed to see the nuggets scattered among the rubbish, and time and the work of others may show that certain methods which I may reject today, or condemn with faint praise, if properly applied, are of value.

Before any judgment may be drawn regarding the value of any form of treatment, clear-cut definition must be made of the condition in which the therapy is applied. It is useless to speak of the value of any form of treatment in pneumonia unless all the cases are sufficiently alike that we may consider this disease a clinical entity. The term "pneumonia," however, is now applied to all those conditions in which there occurs an acute exudative inflammation involving the parenchyma of the lungs. But that leaves us about where we were less than a hundred years ago, in our conception of acute abdominal diseases, when typhoid, paratyphoid, appendicitis, peritonitis, dysentery, and diarrhea were all spoken of as "inflammation of the bowels." The development of pathological anatomy was followed by the grouping of all cases of pneumonia into two forms, one, in which complete lobes are involved, lobar pneumonia, and second, those in which the involvement is irregular and patchy, bronchopneumonia. But today even the pathologist, with the tissues before him, frequently hesitates to say whether the condition from which the patient suffered should be called lobar or bronchopneumonia.

* Read at the Detroit meeting of the American College of Physicians, March 5, 1936.
From the Hospital of the Rockefeller Institute for Medical Research, New York.

From the standpoint of therapy this anatomical differentiation of cases has been of little value, and so far as therapy directed toward overcoming the specific etiologic agents is concerned, it is almost worthless. However, the term "lobar pneumonia" is today well established in medical literature. It would be impossible, even if desirable, to supplant it, but it adds very much to its usefulness if it be limited to cases in which pneumococcus is demonstrated to be the etiologic agent. All the other cases of pneumonia, due to streptococci, staphylococci, etc., may be included under the term "atypical pneumonia," also not a good term, but I know of none better. Today, I shall confine my attention to acute lobar pneumonia, that is, acute pneumococcus infection of the lungs.

For specific treatment, an etiologic diagnosis is essential, but before this is made it must first be determined whether or not the patient is really suffering from pneumonia, and this should be decided as early as possible.

At present, most physicians wait for the appearance of physical signs of consolidation before making a diagnosis. Patient after patient has been sent into our hospital with the statement that he has been suffering with severe symptoms for three, four, five, or even more days, but that the signs of pneumonia have just appeared.

The truth of the matter is that evidence of consolidation is not necessary for the diagnosis of pneumonia. To the experienced observer the symptoms of the onset of this disease are, in most cases, definite and unmistakable. In almost all cases the person who has a chill, fever over 102° , cough, pain in the side, rapid respirations, and, above all, who is expectorating sputum which is bloody or even only slightly tinged with blood, has pneumonia. Even in persons who have suffered from cough or mild upper respiratory infections before the onset, as is the history in 60 per cent of the cases, the appearance of the more serious pulmonary infection is, in most instances, clearly indicated by the more or less sudden appearance of the symptoms I have mentioned. We physicians have made the diagnosis of pneumonia too difficult, and it is much less harmful to make an occasional mistake than to live in fancied security for days until the time when specific treatment would be useful is passed. Most cases *threatened* with pneumonia have pneumonia.

The determination of the etiologic agents in all cases of pneumonia involves difficulties, but in my opinion they are not unsurmountable. Fortunately, laboratory methods are now available by means of which this can be accomplished with little delay. By the so-called Neufeld method, all that is necessary is to treat the sputum with rabbit immune sera of the various types. If, for instance, the organisms are of Type I, swelling of the capsules occurs in Type I serum and in sera of no other types. In probably the majority of cases of pneumonia, the matter is really as simple as this, but not in all, and the physician as well as the bacteriologist must take some trouble and pains. The examination of sputum should be considered an

emergency procedure. It should not be delayed until the next morning or until other work is out of the way.

SERUM THERAPY

Twenty-two years ago at the Hospital of the Rockefeller Institute, we began the treatment of lobar pneumonia with specific immune serum. This was undertaken because evidence derived from animal experimentation indicated that the procedure was theoretically sound. During the intervening years the efficacy of serum treatment in animals has been abundantly demonstrated. Blake and Cecil have shown that monkeys suffering from experimental pneumonia may be cured by the injection of homologous antipneumococcus horse serum, even after the pneumonic process is well established, and Goodner has demonstrated the curative value of immune serum in the much more susceptible rabbits, even when the administration of serum is delayed as long as 72 hours following infection.

But demonstrations in animals are not sufficient. We must know by actual experience whether or not serum treatment in man is effective. Our first observations in man gave to me very convincing evidence that if sufficient serum be used, and used promptly, true curative effects were obtained in cases due to Type I pneumococci. The evidence was less convincing in the cases due to Type II organisms.

During these years we have treated with serum all cases of Type I pneumonia entering the Hospital of the Rockefeller Institute, except, first, an inconsiderable number of children, most of whom recover without serum; second, patients who were moribund on admission and died before treatment could be instituted; and, third, patients who on admission were manifestly in the stage of recovery. Until two years ago, whole serum in doses of 100 c.c. was administered; during the past two years concentrated serum has been used. As early as 1915, Avery determined which fraction of the serum contained the immune principles, and demonstrated how concentration of the serum might be accomplished. We delayed employing concentrated serum, however, for many years, even after improved methods for concentrating the serum were devised by Felton and others, for the following reasons: In the first place, concentration adds materially to the expense of an already very expensive procedure, since in all methods of concentration a large loss of immune substances inevitably occurs. Concentrated serum contains nothing which the unconcentrated does not contain. In the second place, in our opinion the methods first employed for standardization of the concentrated serum gave entirely misleading information regarding its actual strength. With the methods first proposed, it was claimed that a concentration of twenty or more times that of the original serum had been obtained and doses of 5 c.c. of the concentrated serum were considered adequate. Our own observations and experience taught that this was impossible. Specific treatment in this serious disease is not of the type of a teaspoonful

three times a day before meals. One cannot discuss whether serum treatment, even in Type I pneumonia, is or is not effective. All depends on how it is used. Even at present, its employment is still a complicated procedure, and for its successful use more knowledge is required than that which is given on the wrappers supplied by the commercial houses.

Several years ago, when the New York State Board of Health was able to supply serum concentrated from good effective serum, and not from weak serum which would otherwise be useless, and when we could be sure that it was standardized by a satisfactory method, we began using this, not in doses of a few c.c., but in 15 to 30 c.c. doses. That is, it has been possible to concentrate the serum three to five times. Using the determination of strength employed by the New York State Board of Health, the doses we have used contain 90,000 units.

The greater ease of administration of the concentrated serum is obvious. In addition, most observers feel that the frequency of immediate reactions is less. This, however, is not certain. Anaphylactic reactions may occur with small amounts of serum as well as with large. Febrile reactions depend very much upon the care with which sera are prepared. Certain lots of unconcentrated sera give febrile reactions in a large proportion of cases, others rarely. In our experience, however, using both concentrated and unconcentrated serum from the same source, the febrile reactions with the concentrated serum have been notably less than with the whole serum. Probably the greatest value in using the concentrated serum consists in a decrease in frequency and severity of the symptoms of serum disease. These symptoms occur, however, with either the concentrated or unconcentrated serum, in at least half of the cases, seven to ten days following the administration of the serum. With present knowledge there is no way in which these unpleasant but harmless symptoms may be completely avoided.

In our clinic 462 cases of Type I pneumonia have now been treated with immune serum. Its value has been judged by the apparent effect on the symptoms, the rapid appearance of immune substances in the blood, the fact that following its administration bacteria disappear from the blood, and on the mortality rate in the patients treated.

Of the 462 treated cases, 48 died, a mortality rate of 10.5 per cent. Since, during the same period, the mortality rate in cases of pneumonia not due to Type I pneumococci has remained at about the same level as that of other hospitals, it seems that the low rate in Type I cases is definitely dependent upon the serum treatment employed.

All cases admitted have been treated as soon as the diagnosis was made. This is of importance because some of those employing serum have recommended that it be used only in cases that can be treated as early as the third or possibly the fourth day. It is true that the effectiveness of the serum is apparently greater the earlier in the disease it is used, but our experience indicates that no patient, however late he is seen, should be deprived of the benefits of this measure. In this series the mortality rate in cases

treated during the first three days was 4.8 per cent; in those treated on the fourth day or earlier, 8.2 per cent; on the fifth day or earlier, 8.6 per cent, and in those treated after the fifth day, 19.5 per cent.

In general, our earliest conclusions regarding the value of Type II serum have been confirmed: namely, that it is not sufficiently effective to justify its general use. Sera for treatment in cases due to pneumococci of some of the higher types have now been prepared, and the results with some of them seem to be good, but the experience as yet is not sufficiently large to permit conclusions to be drawn. It is not impossible that with improvements in methods even Type II serum may be made useful. Type III pneumococci differ from the others in their immunological properties, and it is probable that if specific treatment in cases due to these organisms can be developed it will have to be based on different principles. The complaint is sometimes made that, after all, serum treatment is possible in only a part of the cases of pneumonia, and attempts are made to treat all cases either with Type I sera or with so-called polyvalent sera. Type I pneumonia, however, in this country probably causes 25,000 deaths every year, more than twice as many as were ever due to typhoid, even when it was most prevalent. Type I pneumonia should be looked upon as a specific infectious disease, as specific as is typhoid fever, and be treated as such.

From our experience, therefore, Type I serum should be given as early as possible and in large amounts, and the doses should be repeated every four or five hours until definite effects are seen in the fall of temperature, decrease in pulse and respiratory rates, and improvement in the other signs of intoxication. It is better to give too much than too little. Skin tests with soluble specific substance, as proposed by Francis, are useful in determining when sufficient serum has been given, but the observer must have had considerable experience in order to rely on this method alone.

Much stress has been laid upon the possible dangers of violent reactions. There are some risks, but it is now possible to guard against them. That disastrous results did not occur when we first began using very large amounts of serum intravenously, when we did not know the dangers or how to guard against them, shows that the dangers are not too great. By making preliminary tests for serum sensitiveness, by proceeding very slowly in the first injection, and by prompt use of adrenalin in case any symptoms occur, the possibilities of serious serum complications are almost entirely avoided.

CHEMOTHERAPY

The only other form of therapy at present employed in overcoming the infectious agent consists in the use of chemotherapeutic agents, such as optochin and other quinine derivatives. While studies made by Morgenroth and others have demonstrated that in mice infected with pneumococci definite curative effects may be obtained, experimental and clinical studies made in our clinic and elsewhere have shown that in man, in order to obtain

sufficient concentration of the drugs to be effective, such large doses must be employed that toxic effects, notably amblyopia, occur, and that the use of these drugs in human therapy is therefore unjustifiable.

It hardly seems necessary to discuss vaccine treatment, since at present it has no experimental or theoretical justification.

GENERAL MEASURES

Apart from specific therapy, however, the physician is not entirely without weapons in the struggle with pneumonia, though it must be admitted that they are not very powerful ones.

Possibly the most important measure is rest. In the last analysis it is always the patient himself that must overcome the infection, even with the aid of serum, and everything that conserves the patient's strength is of importance. The first advice to be given to patients with pneumonia, even though they do not appear very ill at the onset, is to keep as quiet as possible. The second important point is to reassure them. Fear is as serious an element in the battle with pneumonia as we are told that it is in a financial depression.

MORPHINE

Something may be accomplished with drugs in allaying restlessness, but the ideal drug for this purpose is still to be sought. Formerly I was of the opinion that morphine was of much value in the treatment of pneumonia, and my clinical experience still leads me to believe that, especially in patients with severe pleural pain, in the early stages of the disease, there is no other drug which will so satisfactorily allay the general restlessness and permit the conservation of strength and energy. In view of the more accurate studies of Davis made in our clinic, however, we have become much more conservative in its use. It was found that in most cases following its administration there occurred not only a slowing in respiratory rate, but also a diminution in pulmonary ventilation and a decrease in oxygen saturation of the arterial blood. These changes were not striking, however, and it was found that when the depth of respiratory movements was diminished on account of the pain, the relief following the administration of morphine might result in actual increase in the pulmonary ventilation. In cases of extensive pulmonary involvement with diffuse moist râles, however, the administration of morphine at times resulted in a marked degree of anoxemia.

OXYGEN THERAPY

Probably the most striking functional change seen in pneumonia is rapid, shallow breathing, with deficient saturation of the arterial blood, as indicated by cyanosis. So far no satisfactory specific method for increasing the pulmonary ventilation has been found. The usefulness of breathing air containing an increased percentage of carbon dioxide has been much recom-

mended, but in our experience this procedure has not given significant therapeutic results. While the anoxemia bears some relation to the rapid and shallow breathing, it is probably related in greater measure to the impairment of the respiratory surface of the lungs, especially where there is much fluid exudate.

Twenty years ago, although the inhalation of oxygen in various pathological conditions had been long employed, the value of this procedure was much in doubt, and certain physiologists even claimed that on theoretical grounds its administration was useless. To attempt to settle this question, there was built in the Hospital of the Rockefeller Institute a chamber in which the oxygen content of the air could be regulated, and in which patients suffering from pneumonia could be treated. The results in the relief of cyanosis were so striking that since then numerous chambers in various hospitals have been constructed, and many other devices for increasing the oxygen content of the air breathed by the patient have been designed.

So far as simplicity of operation, comfort of the patient, and convenience as regards nursing are concerned, there can be no doubt that the chamber is *par excellence* the method of choice. But the initial expense is great, and chambers are not generally available. Tents have now been perfected so that in them it is possible to maintain a constant atmosphere at an even temperature almost as satisfactorily as in the oxygen chamber. The nasal catheter method is useful, but is to be recommended only when no other method is available. Recently a very ingenious and simple method of administering oxygen has been devised by Dr. Burgess of Providence. This consists merely of a box, open at the top, lined on the sides and bottom by a rubber bag attached by clamps to the upper edges of the box. At the front is an opening in the rubber bag through which the head is thrust, the edges of the opening fitting tightly about the neck. In the bag near the bottom are openings for tubes through which oxygen is allowed to flow continuously. The oxygen diffuses only slowly upward, so that with a flow of four to six liters per minute the air in the bag at the level of the patient's mouth and nose can be kept constantly at 40 to 50 per cent of oxygen. With a satisfactory cooling system, the apparatus can be employed continuously without discomfort to the patient.

In our earlier employment of the oxygen chamber we determined whether a patient should be treated by this method or not by making actual measurements of the degree of oxygen unsaturation in the arterial blood. It has been found, however, that the degree of cyanosis present is a sufficiently accurate indicator.

Our custom is to maintain an atmosphere in the chamber containing 40 to 50 per cent oxygen, usually 40 per cent. Others advise higher concentrations, but it must always be borne in mind that very high oxygen atmospheres are toxic. There seems little use in increasing the oxygen to a level higher than that necessary to relieve the cyanosis. It is not likely that placing the patient in the chamber for short periods of time is of any value. Having

once placed a patient in the chamber, it is our usual custom to keep him there until the acute intoxication is over, and then to bring about the change to usual atmospheric conditions very gradually.

It is very difficult to evaluate the actual benefit derived from the use of oxygen. While, by an occasional patient, much subjective relief is obtained, in most instances this is not evident. The immediate effect on the character and frequency of respirations is not so great as certain of the reports would lead us to expect. What the effect may be on the final outcome cannot be stated at present with any degree of accuracy. Contrary to the statements of other enthusiastic observers, I can only say that our mortality in cases not treated with serum has not notably diminished since the introduction of the oxygen chamber. Nevertheless, we should feel greatly handicapped if we lacked facilities for supplying oxygen to patients with cyanosis.

SODIUM CHLORIDE

Another physiological alteration in patients with pneumonia is a decreased excretion of chlorides in the urine and a diminution of the chloride content of the blood plasma. From time to time during the past 25 years, papers have appeared dealing with the saline treatment of lobar pneumonia. Recently attention has been drawn to the fact that both in lobar pneumonia and in pyloric or high intestinal obstruction the chloride content of the serum is decreased. It has been found that the administration of large amounts of salt-containing fluid to patients with obstruction or to dogs in which the condition has been produced experimentally results in a marked decrease in the intoxication and prolongation of life, and this has been used as an argument in favor of administering sodium chloride to patients with pneumonia. It is doubtful, however, whether there is justification for drawing this analogy too closely. It has been shown that the loss of chlorides in obstruction is directly related to the vomiting of the high chloride-containing gastric contents. The loss may be enormous, and loss in water may be correspondingly great. Under these conditions it is not surprising that replacement of the salt and water may be very beneficial.

On the other hand, the diminution of chlorides in the blood in pneumonia is minimal compared with that occurring in obstruction. Moreover, in patients that have been given 15 to 30 gm. of sodium chloride per day, there is little evidence that the chloride content of the blood has been increased to normal amounts. Certain writers are very enthusiastic about this form of therapy. Other good observers are more cautious, but still believe advantageous results are obtained. Influenced by these opinions, we have given certain of our patients moderate doses of sodium chloride daily and have thought that, in some instances, abdominal distention was thereby diminished, and some decrease of the symptoms of intoxication was observed. It will require much wider experience definitely to decide these questions. One of Sunderman's patients developed subcutaneous edema

when receiving 15 to 30 gm. per day, and other observers have noted the occurrence of pulmonary edema. Large doses should, therefore, be avoided. Our patients have received not more than 10 to 12 gm., usually 5 to 8 gm., in addition to that in the diet daily. The salt is given in capsules. Frequently nausea and vomiting result. McCann recommends that in serious cases 10 to 15 per cent NaCl solution may be given intravenously. Thirst is frequently increased following the administration of sodium chloride, and therefore the administration of fluids is facilitated. In so far, at least, the method is useful. In all cases of pneumonia, the attempt should be made to administer at least 3,000 c.c. of fluid daily. If the patient will not or cannot take this amount, it may be given in the form of normal salt solution intravenously. Additional calories may also be given by adding glucose to the salt solution.

At the present time the administration of sodium chloride to pneumonia patients should be considered to be in an experimental stage, and the basis for this form of therapy largely empiric. One must always remember that modification of physiological alterations present in disease does not necessarily increase the patient's chances of recovery. Most of us remember when antipyretic drugs were in their heyday. Today, fever is being produced artificially in attempts to cure certain infectious diseases.

DIGITALIS

Much has been written about circulatory disturbances and about the failing heart in pneumonia. Contrary to the usual opinion, my own experience has led to the view that the early intoxication in pneumonia rarely manifests itself by injury to the heart, and that circulatory inefficiency is usually a late manifestation of the disease, occurring at a stage in which drugs can be of little value. Most patients die in pneumonia, not from cardiac failure, but from disturbances in respiration. Observation of the character of the breathing (frequently gasping and shallow, with laboring of the muscles of respiration) gives much better prognostic information than measuring the blood pressure. Of course, in the later stages of pneumonia, gradual lowering of diastolic pressure with loss of tone in the peripheral vessels and signs of cardiac dilatation do occur.

The question of the employment of digitalis in pneumonia is not yet entirely settled. In 1916, on account of the considerable number of pneumonia patients showing cardiac irregularities, and because of the known danger of attempting to digitalize the heart rapidly, the method of giving all pneumonia patients moderate doses of digitalis was introduced into our clinic. In 1930, however, Niles and Wyckoff reported that in a large series of cases treated with digitalis, the mortality was considerably higher than in a corresponding series of cases receiving no digitalis. In the light of this experience, Cohn and Lewis carefully reviewed all our cases. The conclusion reached was that giving digitalis did not seem to influence the course of the disease. As a result of these studies we have discontinued the

routine use of digitalis, employing it only under conditions, such as auricular fibrillation, where it would ordinarily be employed, even though no pneumonia were present, and then in exactly the same manner.

In cases where there is a progressive fall of the blood pressure, it is our custom now to rely on intravenous infusions of normal salt solution with, if necessary, injections of ephedrine.

It is needless to discuss here the other drugs that have been used in the past to stimulate the heart, frequently as a routine, before any signs of cardiac weakness have appeared—caffeine, strychnine, camphorated oil. Today I think there are few advocates of this form of therapy.

QUININE AND ALCOHOL

Besides these measures, intended to relieve certain symptoms and to overcome definite physiological alterations, numerous methods have been proposed which are supposed to have a definite action on the infectious process; the nature of the action, however, not being understood at present, or only explained by theoretical considerations. Ever since pneumonia was first recognized, modes of treatment have appeared, flourished for a time, and then disappeared. One has only to recall the vogue for blood-letting which flourished in waves from the time of Hippocrates, had an enormous vogue in the seventeenth century, and was still recommended and even somewhat widely employed in my own early medical days. There were periods in which failure to bleed and actively purge with tartar emetic was ground for malpractice suits.

Certain drugs, as alcohol and quinine, have been thought to have a specific action in this disease, and are still employed by certain physicians. I have had little experience with the intensive use of quinine, but early in my medical life saw patients treated routinely with large doses of alcohol. My recollections of this experience are not pleasant. It is generally held that in alcoholic patients it is wise not to discontinue its use completely, and this seems sound and is the custom in our clinic.

Other measures which have a vogue today and concerning the value of which the evidence is more or less conflicting, are diathermy and artificial pneumothorax.

DIATHERMY

Several years ago, influenced by the reported favorable results from the use of diathermy, Binger and Christie in our clinic carried on studies with the idea of determining its value. During the passage of the diathermy current they made direct measurements of the temperature which developed within the lungs in dogs, both in the lungs of normal dogs and in those which were the seat of a pneumonic consolidation. It was found that in normal lungs in no instance was it possible to demonstrate any considerable amount of local heating, the explanation being that the lungs represent an excellent watercooled system, and that the intact pulmonary circulation

prevents any considerable degree of local heating. In consolidated lungs of dogs, probably because of the disturbed circulation, it was possible to increase the local heating slightly, but not more than one or two degrees. In three pneumonia patients direct measurements of the lung temperature were made by the aid of thermocouples enclosed in an ordinary Luer needle, which was inserted directly into the consolidated lung. In none of these patients was there an appreciable rise in lung temperature during or after exposure to the diathermy current.

In the light of these studies, no further clinical use has been made by us of this method of treatment. One hesitates to state categorically that this method has no value. We grow cautious with experience. One can only say that it is not based on experimental or clinical studies that appear to be sound. Even though it were possible to raise the temperature within the lung, it would not necessarily follow that the results would be beneficial.

ARTIFICIAL PNEUMOTHORAX

Although artificial pneumothorax as a therapeutic procedure was carried out in a few cases of pneumonia in 1919 to 1922, the method was not employed to any considerable extent until within the past two years. The chief justification for its employment is that offered by Friedman, who stated that by the collapse of the lung a state of immobility or rest is produced which diminishes the absorption of toxic products, and promotes healing. At the same time the inflamed pleural surfaces are separated; thereby pain is relieved, enabling the patient to breathe more deeply and also to obtain mental and physical rest.

Most of the clinical reports, so far, have concerned small numbers of cases, and usually only moderate amounts of air were injected. The most extensive and careful study has been that of Blake in 42 cases. He has drawn attention to the fact that to obtain immobility of the lung it is necessary to inject sufficient air to produce complete collapse. He studied his cases by roentgen-ray examinations and found that the amount of air necessary to produce complete collapse varied greatly in different patients, and could not be predicted, but usually varied from 1800 c.c. to 2400 c.c. From a study of his cases it is difficult to judge whether or not the procedure had a favorable effect on the outcome. He rightly avoids drawing conclusions from the mortality rate in such a limited number of cases. However, 10 of the 42 patients died. There is, on the other hand, no evidence that the treatment was harmful. In only one of the cases treated before 72 hours after onset did spread to the opposite lung occur. He speaks of the excellent therapeutic results in the early cases without interfering adhesions, but only 10 of his cases belonged in this category and he concludes that "the use of this operation as a therapeutic measure in selected cases is worthy of further trial."

In our clinic at the Rockefeller Institute, a small number of cases has been treated by this method, and a clinical report on nine thoroughly studied

cases has been made by Abernethy, Horsfall, and MacLeod. Since this report, 13 further cases have been treated, making 22 in all.

Confirming Blake's observations, it was found that large amounts of air were necessary to produce collapse of the lung and immobilization. Pleural pain was relieved, but in many instances where large amounts of air were injected there developed dull, aching substernal pain that at times was as distressing as the sticky pleural pain had been. Moreover, in some of these cases, there occurred an increase in the dyspnea, tachypnea and cyanosis. While no permanent harmful results could be demonstrated, the procedure could not be shown to exert any favorable influence on the course of the disease. In the more recently treated patients, only small amounts of air, sufficient to separate the pleural surfaces, have been injected, and in most instances the relief of pain has been definite.

Although apparently so far no serious results have followed the production of pneumothorax in patients with pneumonia, the method is not without its dangers. In two of our cases apparently rupture of the lung occurred, with the development of very high intrapleural pressure and widespread subcutaneous emphysema. Both of these patients were subjects of chronic pulmonary emphysema and the operation should probably not be undertaken in such persons. In five of our nine cases treated by complete collapse, there developed an accumulation of fluid in the chest, but in only two was it sufficient in amount to require aspiration. While empyema has developed in a number of the reported cases, this has not occurred as frequently as might have been anticipated.

While carrying out this procedure in pneumonia is not a serious or difficult operation, it is not one to be lightly undertaken by anyone who has had no previous experience with the technic of artificial pneumothorax.

CONCLUSIONS

From this brief review it seems evident that the only form of specific therapy proved to be useful and available at present is serum treatment in Type I pneumonia. Etiologic diagnosis should be made as early as possible and treatment started without delay. Care should be taken to have good serum and it should be administered in large amounts and its use continued until recovery is evident. Certain measures, such as the administration of oxygen and of sodium chloride, may be useful in overcoming pathological variations in the body mechanism.

The value of artificial pneumothorax awaits further study. At present its usefulness seems to consist in the relief of pain rather than in any effect on the infectious process. Finally, it should be stated that, while the solution of the pneumonia problem has not been reached, some advance has been made in the past twenty-five years. Not the least important part of that advance has consisted in the increase of knowledge concerning the nature of the disease and of the natural mode of recovery. The accrued knowledge should lead to acceleration of progress in the development of methods of treatment and cure.

THE RÔLE OF THE PERSONALITY IN PSYCHOTHERAPEUTICS *

By AUSTEN FOX RIGGS, M.D., F.A.C.P., and HORACE K. RICHARDSON,
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A psychoneurosis is an involuntary and automatic disorder of normal people, based on hypersensitiveness and the relative imbalance of instincts, causing inner conflict between instinctive forces and adult, intelligent strivings and ideals. Some outward maladaptation to life manifests itself by typical symptomatology in the vegetative, somatic, emotional or intellectual fields, thereby functioning as a compromise between the demands of the instinctive forces and the higher intellectual and ethical aims, and as a protective mechanism against whatever is painful and unacceptable emotionally and intellectually. The particular form of neurosis which develops is determined by the relative composition of individuality and environmental experience.

The importance of the situation in the origin and development of the psychoneuroses has been forcefully and accurately demonstrated. While it is a recognized fact that certain types of situations in life are common to the origin of all cases of nervous illness, they are recognized as the precipitating causes only. They constitute an extremely important factor in the development of the various types of maladaptation, however, and may give the key to an understanding of the nature of the case, be the determinants of the ultimate prognosis, and indicate the pattern of the therapeutic approach. We believe, however, that the fundamental causes of the psychoneuroses lie within the individual himself in the form of a specific hypersensitiveness to sensation or to emotion, or to both.

The treatment of the psychoneuroses consists of three major efforts, namely: (1) to disclose to the patient the original causes of this hypersensitiveness, including those of a basic constitutional nature; (2) to assist him in the development of insight into the origin, nature and function of the maladaptive reactions; (3) to use this understanding of the fundamental qualities of his personality as the foundation upon which to erect a more efficient plan of living. We believe that the origins of the psychoneuroses lie in the phylogenetic and ontogenetic development of the structure of the personality, and therefore constitute the essential guide to the therapeutic approach in each case. Hence, we shall devote the remainder of this paper to a consideration of this aspect of psychotherapeutics.

At the outset we must presume the acceptance of the principle of psychological integration in contradistinction to the pedantic attitude of parallelism, which implies a theory that mind and body "accompany each other

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but are not causally related." For many centuries man looked upon himself in terms of biological fragmentation. Isolated manifestations of his personality occupied his attention for certain periods of time to the temporary exclusion of all others. Sherrington, in 1906, brought out his inspiring work on the integrative action of the nervous system and forever changed this attitude of incompleteness. Adolf Meyer accomplished an even more useful piece of work when he emphasized the pragmatic significance of this principle of integration in the higher mental functions and between the various physiological and psychological levels. This implication not only assumes a relationship of structure, but includes as well a unity of action even more closely organized than the structural systems themselves. There is an interdependence and synthesis of function and action that frequently transcends our knowledge of nervous system localization, and even in the presence of disease processes and disorders of function, we still witness the evidence of an organized whole. This often persists in spite of partial disintegration in certain parts of the organism, either structural or functional. In spite of the great individual differences among various people, we always find this fundamental principle of integration as the major factor in the total organization of the human personality. The ideal of mental health is based upon this unity of the personality. In any therapeutic effort, therefore, this ideal is the basis for the development of an understanding of disintegration, as well as integration, and until the former is investigated subjectively and understood by the patient, the subsequent steps of psychotherapeutic effort leading to integration cannot be comprehended, and their value is lost to the patient. Unless each of the antecedent steps in this synthesis is fully understood by the patient himself there will be a succession of corresponding faults in the later stages of his understanding, and in his ability to synthesize all of its factors. We believe, then, that a review of the biological and developmental factors of his personality constitutes the first and most fundamental parts of the plan of reëducation.

There have been many overlapping classifications and descriptions of personality attempted. No two psychologists would agree as to its basic structure, its exact definition or its fundamental characteristics or distinctions. Study and observation by many individuals have resulted in an encyclopedic accumulation of facts and theories relative to the personality and its reactions and expressions. Frequently the terms "personality," "individuality" and "character" are confused and used indiscriminately.

Jung's concept of introvert and extrovert personality is altogether too restricted, and does not appear to give consideration to immediate antecedents. Kretschmer's plan of pyknic and asthenic types, although based upon biological and constitutional fundamentals, involves a typing of personality rather than an explanation of structure. It implies a consideration of character. Character is not a fundamental part of personality; it is an expression of it. Freud, aside from his overaccentuation of sex and the rôle of the unconscious, came closer to what we believe to be the truth in his

"Id-Ego-Super-Ego" idea, but he apparently minimized the essentially organic or physical elements in personality. Adler, in his individual psychology, is altogether too stereotyped and teleological, and, like Jung, disregards immediate antecedent circumstances. There are many other theories, but in our opinion they are more or less impractical because they do not carry causal implications.

It is our belief that the most useful and accurate concept of the personality structure is that based upon the theory of the psychobiological development of the animal kingdom from its beginning to the present. We believe that each individual personality is made up of the end-results of development, the residuals of growth and experience, integrated into certain actual and potential constituents which express themselves in four predictable types of specific reaction. These reaction types, the reflex, the instinctive, the intelligent and the ideal, are based on four developmental neurological levels of the nervous system. These four levels of reaction represent four major developmental epochs of the entire animal kingdom from the ameba to man, and therefore explain the purely biological foundation of the concept. They are repeated in the development of the individual from birth to maturity, and supply an adequate background for understanding both the mature and the immature aspects of personality. They explain the phenomena of personality disintegration and retardation, and give a foundation for comprehending the antecedents of individuality and character. These reactions include the physical, emotional, mental and moral dynamic forces of life, which vary in relative strength in each individual. They undergo many specific modifications through certain conditioning influences of life from childhood onwards, and thus give us a basis for comprehending individuality and furnish adequate explanation for the antecedents and motivations of all types of psychoneurotic maladaptation. When these reactions are considered in the light of individual hypersensitiveness, they explain the degree of the dynamic responses. This concept not only satisfies the biological point of view, but has proved satisfactory in the understanding of the origins and determinants of psychoneurotic maladaptation, and in addition furnishes a convincing foundation upon which to erect a successful system of psychotherapeutics. It stands the practical test of experience. This concept bears a certain superficial resemblance to Freud's more recently developed figure of "Id-Ego-Super-Ego," which, however, is more apparent than real. Any question of its priority is settled for all time by the relative dates of publication. It was published in 1912, while Freud issued his book in 1921.

The first of these developmental levels, the reflex, represents the lowest type of biological adaptation as implied in the functions of the primitive brain stem, a stage of biological growth when the neurological elements were relatively simple. It is a purely physical or somatic type of response and does not imply a "mental" reaction as commonly understood. This type of response implies all those primitive, non-affective responses which occur outside of awareness, and which, through the process of conditioning and

repetition, have become incorporated into automatic neurologically determined functions. In this evolutionary stage there had not yet appeared any of the so-called higher functions of feeling or thinking. At this level are found those phylogenous influences commonly included in Jung's concept of "the collective unconscious." This primitive structure in man is represented in general by the spinal cord and the medulla. It is at this level that the constitutionally determined element of sensitiveness first appears. An understanding of the elementary functions and expressions of this level of reaction upon the part of the patient is necessary, and the development of this understanding is one of the first steps in the therapeutic excursion.

The second type of reaction is due to the development of the next higher level of neurological structure, the diencephalon, which, in the words of Tilney and Riley, "gives rise to the thalamus, the hypothalamus, the epithalamus and the metathalamus." When this region in the brain developed, there arose a new type of reaction known as the "instinctive." These instinctive tendencies are the raw forces at the bottom of man's behavior, so to speak. They function from birth to death. Some of these forces have to do principally with the individual's survival, with his security as an individual. Others function as forces which insure the procreation of the race, others for the welfare of the race en masse. Each instinctive reaction is as it is because of the individual's inherent structure and the functional organization of that structure. Man is timid and pugnacious, socially inclined, hungry, sexually susceptible because he is built that way and organized that way—born to react that way. But each man is apparently born unequal so far as the relative strength of the instinctive tendencies is concerned. Some men are "naturally" more pugnacious than timid, some more dependent on their fellow man, some more self-assertive than others and so forth. Many of these relative differences are observable at birth or very soon after; in short, before environmental experience could reasonably be supposed to have modified the raw material to any great extent.

Instinctive reaction is not, however, a simple mechanical reflex even in its primordial raw form. It involves the whole creature, his whole biophysical organization, together with many complex reflexes and is accompanied by much activity that does not necessarily appear on the surface, as has been ably demonstrated by Cannon. For instance, if the instinctive tendency to self-protection is aroused, there is a quick mobilization of all the physiological forces appropriate to escape. Almost at once the animal, be he man or rabbit, finds himself in the best possible condition for flight. The muscles of locomotion have become tensed, the circulation carries to them blood freshly loaded by the endocrine glands with material for the most effective and efficient action. Respiration is doing its part to keep the blood stream thoroughly oxygenated. The gastrointestinal tract's activities are throttled down to a condition of relative paralysis. Other physiological changes have taken place, all functioning in the same direction, until the creature is in an ideal state for the instinctive action of escape to take place.

While all this is going on, it is of course inevitable that the creature must be conscious of at least a large part of these changes. He is no longer comfortable, in fact he is distinctly uncomfortable. He may be aware of his dry mouth, of his rapid heart beat, of his trembling, tense muscles, but even if he is not aware of these specific items, he is at least aware of the sum total of the changes that have occurred in his bodily sensations, so that he *feels* a painfulness and at the same time as part of that uncomfortable feeling, a strong desire to escape, to discharge that mobilized energy and to rid himself of the discomfort as fast as possible. In short, when the instinct of escape is aroused, the creature is not only mobilized for escape, but *feels* that mobilization as a strong emotion accompanied by an intense desire to flee.

Thus an instinctive reaction may be said to have three parts just as the simple reflexes have three parts—the sensory, the central adaptor and the expressor or motor part. Each instinct can also be said to be accompanied by its own appropriate emotion which is either painful to some degree or pleasant to some degree, and which besides its pleasure or pain element has a second strong motivating force within it, namely, the desire to escape from or approach the object which has aroused it.

The instinctive make-up of an individual is the second structural element of his personality and individuality. Therefore, to understand him it is necessary to gauge as nearly as possible what the relative strength of instinctive forces in his inherent makeup may be. Is he more pugnacious than timid? Has he a relatively strong or weak social drive? Is he more self-assertive or more retiring than self-important? Has he a relatively strong or weak sex drive? Is he more or less suggestible than the average? By suggestible is meant the degree to which he is liable to the uncritical acceptance of ideas. It is an instinct-like quality present to some degree in everyone, usually greater in youth than in adult life, and varying in regard to any subject in inverse ratio to the amount of the individual's knowledge of that subject.

The development of insight upon the part of the patient into the nature of these instinctive reactions, especially those that have contributed largely to the origin of his own conflicts, is the second logical step in the development of the therapeutic teaching.

The third type of biologically determined reaction is the intelligent. It came about as the result of the further development of the telencephalon or end brain. Growth in this part of the central nervous system brought new capacities and abilities, a new function and a new type of reaction to the various stimuli of life. Just what intelligence is we do not know. The word is used very widely and as loosely as most psychological terms. Let us limit the meaning for our present use to its functional significance rather than to attempt a definition. Let intelligence mean the ability to understand, to comprehend whatever our senses bring to us and to judge of its significance. Let us add to understanding and judgment one other related sub-

function, namely, choice, which is the executive function of intelligence, and then the description will be sufficient for our present purpose.

Obviously individuals vary widely in regard to the quality of intelligence they possess. Here again men are born unequal, some extremely well endowed, some with only an average endowment, and others poverty-stricken from birth. From the quantitative point of view alone then, intelligence is one of the fundamental variants determining the individuality. This characteristic varies greatly within the normal, but more in quality than in quantity. It would seem, in short, that people differ from each other even more markedly in the specific type of intelligence they have than in just how much of that master function they possess. One need only mention the vast differences among children, the mechanically minded, those who take to mathematics with marked ease, while others are "born linguists," to appreciate how important a variant within the normal this qualitative specificity of intelligence is in the equation of individuality.

These variations in the fundamental and functional, the inherent and acquired intelligence are of at least as great import to the understanding of any individual as the variations of instinctive make-up, for by virtue of the former his mode of adaptation to his world will be very largely determined.

In the ability to understand, to judge of the significance of things and to exercise choice, is observed the great adaptive control of all the foregoing primordial forces. It is that which enables us to understand our environment, our relation thereto, and last but not least, to choose among all the possible plans of action the one most likely to give us the results we desire. It is this faculty par excellence which constitutes man's ability to make his adaptation purposive, and this raises it from animal reaction to human behavior.

Finally there comes the fourth or highest level of the adaptive machine as represented neurologically by the growth and development of the neopallium. This level is known as the ethical and it is here that the most difficult integration takes place. Man's demand for the specific form of satisfaction and happiness which ethical conduct engenders seems to be a genuine biological development. Is it not indeed this very demand in each individual which makes civilization a biological necessity? In early time, the instinct of self-protection underwent modification when man began to live in groups and the safety of the group had to take precedence over the survival of the individual as each man's objective, and thus simple society became a sort of mutual protective association where each individual was classified according to his material value to the group. A sense of individual responsibility toward every other member developed, probably the expression of a strong instinctive force released by the absence of the necessity for self-protection, which grew as part of the progress of society toward civilization. This desire to protect, this responsibility for the welfare of the other fellow no doubt spread from its earlier exclusive application to

members of the individual's own group, until it included those of other groups and finally, as an ethical idea, became all-embracing.

However, the ability of the individual human being to function ethically is apparently acquired through training, example, education and other forms of experience, for although there is an inherent drive in this direction, the acquirement of it takes many years, beginning in infancy and continuing into old age, at least to a diminishing degree. It is upon this level that the unified energies of man come to fruition in the form of purposive striving and it is here that man erects his philosophy of life.

An item which affects individuality very definitely and which varies greatly even within the normal is mood. Let it be understood that by mood is meant the general tidal level of affective activities, the height or depth of the feeling level. The top of the tide represents the mood of exaltation and a full moon flood tide, transcending the normal, will represent manic elation. The ebb tide, on the other hand, pictures gloominess, blues, and the extreme ebb, beyond the normal, would represent the depressed phase, the melancholia of a manic depressive episode. But well within the normal there are mood swings both up and down sufficiently marked to affect not only feeling but thought and action as well. Normal people vary from each other in the degree to which they are subject to mood swings and also as to whether these swings are habitually up or habitually down, and as such mood swings tend invariably to affect both thinking and acting, they can neither be ignored in understanding an individuality nor neglected when dealing with a person's difficulties in adaptation.

There is one all-qualifying item in the equation of individuality which, according to our present formulations, comes neither under intelligence nor instinct, but, nevertheless, has to do with both and with every other characteristic of every human being, and that is temperament. This word has been used so freely and so carelessly not only in common parlance by the man in the street, but also in psychological literature that it may connote anything from the sum total of human characteristics "to an overworked alibi for being dirty, careless and never paying one's bills." So here again we must limit the meaning of the term to something definitive and practical. In this case let temperament equal sensitivity and, to be more specific, let it equal that particular degree of sensitiveness to the painful or pleasurable in sensation and emotion, thought or mood possessed by an individual. Even shortly after birth it can be observed how infants vary in acuity and completeness of reaction to stimuli both internal and external. Even babies manifest a degree of sensitiveness so that "he who runs may read." It is almost equally obvious in adults in spite of the modifying influence of experience and training, for in them that sensitiveness to the pain-pleasure element in experience has already become highly specialized, highly specific. In short, through experience this sensitiveness becomes specific to the instinct or instincts which are inherently relatively overactive or which have become so through experience. Therefore, the finished product will manifest his

sensitiveness in particular and often easily observable directions. This sensitiveness is a very real thing physiologically as well as mentally. For instance, a hypersensitive person who is at the same time more timid than pugnacious not only needs more courage to achieve even ordinary aims, but will show his sensitiveness to fear not only in the necessity of more than ordinary courage but in the aggravations of the physiological reactions characteristic of fear. These may manifest themselves in disturbances of the gastrointestinal tract or of the heart's action, by sweating or by blushing and blanching, or in short, by undue disturbance of any or all of the functions under the dominion of the sympathetic system.

Obviously the effect of variation in this characteristic upon the individuality as well as upon the technic of the person's adaptation may well be striking. The part that it plays in normal life, its functions as an asset, as well as its rôle in psychoneurotic maladaptation, its liability aspect, is one of the main concerns of psychotherapeutic treatment.

To recapitulate briefly, the component parts of personality and their respective neurological levels are:

First, the level of vital reflex under the dominion of the medulla.

Second, the primal inherent forces called instinctive in which we follow very roughly McDougall's classification—instincts which serve self and those which serve race and species, represented on the neurological level by the thalamic region of the brain.

Third, intelligence, that characteristic which modifies or adapts the primal forces to a wider, more elastic and diversified use, represented neurologically by the fore-brain.

Fourth, the super-intelligent or ethical level, represented by the latest and most complex development of the fore-brain, particularly by the frontal lobes.

Finally, to complete the picture of individuality, we must include mood, temperamental-sensitivity, items which directly qualify the primal forces, as well as intelligence, by affecting the quality and intensity of their action.

These are the variables in the human equation which in their reaction to one another and through their organization as a whole constitute the bio-psychological entity, the individual, who in ways that are characteristic of the race, on the one hand, and of himself individually on the other, reacts to his environment and to which the environment reacts.

These four levels of biological development, which represent the evolution of the adaptive processes of the animal kingdom, are repeated in the growth of each individual. They must be studied in regular order and thoroughly understood by the patient before he can comprehend the various factors that have preceded his maladaptations.

At birth this machine is imperfectly developed and immature, and, therefore, functions only in part. The process of maturation is determined and affected largely by the nature and character of the environmental influences, i.e. the stresses and disciplines which surround the growing child. On his

way toward maturity, the individual may undergo certain experiences, real or imagined, which tend to condition or modify him, to fix his reactions at definite chronological levels and often relegate many of them to the unaware regions of consciousness. It is by this process that the useful experiences of the individual become stored away and made automatic, thus relieving the intelligence of the necessity for repeatedly thinking out solutions for the many new situations that arise in his daily life. It also frees the intelligence and makes it available for use in new experiences and for making adjustments on the purposive plane, but it is also during this process that immature emotional values may be given, more or less permanently, to reactions, which reappear in adult life as though they represented present experiences. Frequently these experiences represent conflicts between the various reaction-levels of the personality and furnish the basis for the origins of the psychoneuroses. Recent environmental situations may reactivate those old emotional values through association and thus contribute to the causes of the maladaptive reactions. Thus it becomes necessary that the individual should possess insight into these motivations, and the development of this insight is an important factor in an effective therapeutic effort.

At birth the normal infant is equipped with a potential capacity for the development of all four of these levels of adaptation. Actually he is largely a mass of reflex reactions, many associational tracts are not yet myelinated and he remains in this condition for a relatively long period after his birth. He is the most dependent creature on earth. He cannot express his needs or his desires in the language of his environment. He cannot move toward the sources of his food supply. He would die of starvation and exposure were it not for the assistance given him in this first stage of his development. He is non-logical because intelligence has not yet developed. He is non-moral, having no group consciousness, and he is completely egocentric and as yet has no concept of "I" or "You." The security of food and protection from the elements are his only needs and are supplied by those around him. Later his psychological needs are furnished by the attention, love and approval of the individuals who constitute the parental group. Because of his immaturity and inability to comply with the laws and customs of this group, the child lives in a world of criticism, admonition and discipline. The first words usually spoken to an infant after the excitement of his arrival has passed is the negative "No! No! Mustn't do that!" Later, these attitudes of constant correction upon the part of the adults (one author calls them "Giants") are frequently unconsciously interpreted as a withdrawal of parental love, or as a possible threat to this love, unless they are balanced by the opposite attitudes. Because of his nature the child cannot mature uniformly and completely without this affection as expressed in approval. He therefore attempts to modify his own demands and conduct, so as to comply with the arbitrary demands of the environment in order to obtain it, in spite of his own wish to act in the opposite manner. He senses, sooner or later, that coöperation with these

external demands brings him the pleasure which the attitude of approval upon the part of the parent excites within him. Parental attitudes, then, become the first and most important factor in conditioning the child's early psychological existence.

As time goes on and the child grows older the instincts become more and more prominent and determine in an increasing degree the motivations of his conduct. As the instinctive desires, needs and demands for gratification become stronger, the greater becomes the conflict between the child and his environment, and the more difficult becomes the solution of the problem of the socializing of his instinctive forces. Eventually the child begins to comprehend the meaning of the contrary attitudes of the parents, but because of the power of the non-logical and non-moral instincts he is bound to have a certain degree of difficulty in complying with them. We tend to forget that he is not just a small adult and expect altogether too much of him. He is but an immature child and he does not yet possess the adaptive machine of an adult. The result of unwise parental attitudes is repression. The more severe the parental authority and the more sensitive the child, the more numerous and deeper become the repressions, or the more violent are the rebellion and resentment against parental authority. The more exaggerated and persistent the authority, the more the repressions become charged with overdetermined emotional values.

Because of the rapidity with which each new experience comes to the child, and the necessity for learning quickly the difficult business of adaptation, there are many experiences which are thrust into the realm of unawareness in an unfinished condition and partly or wholly forgotten, although the emotional force attached to them may remain active. The child mind cannot make accurate interpretations or determine correct values in many of these new experiences, and consequently these are stored up in his mind with fictitious values attached to them. These overdetermined and little understood emotional experiences may lie in the unaware region of his consciousness for years in an unfinished and unresolved state and may thus continue to furnish the motives for thoughts and conduct which are frequently inexplicable to outsiders as well as to the individual himself.

There comes a time in the stages of development when an entirely new element makes its appearance in the growth of the personality. Its arrival is not as abrupt as this statement might imply for it makes its appearance gradually and, at first, in minor, simple manifestations. It is the development of the ego or selfhood and occurs at the level of intelligence and at about the same time as the aggressive instincts become more prominent. Self and the awareness of self undergo accentuation, but he also becomes aware of himself not only in terms of the drive of self-importance and self-expression but also as an individual striving for the ethical objectives in his relationship with others. He begins to identify himself with his own kind and tries to act in the manner of an independent adult.

Soon the world of the child enlarges, and he finds himself more or less

on his own in contact with people both young and old outside of his own immediate family group. The child is at first confused by the apparent disagreement between his formerly unquestioned parental authority and the actual facts of life as he now observes them. Here before his eyes is another child doing the very things prohibited by his own parents, and escaping the punishment which he had learned to expect. What does he do? He begins, with much trepidation, to use his newly acquired ego and its correlative intelligence. He begins to experiment. He begins to use his new aggression. To his amazement he discovers that he also escapes the consequences predicted by his parents. Thus he goes through a period of disillusionment and reevaluation. He discovers that certain laws set up by the parents are not universally accepted and that certain parental attitudes and opinions are not necessarily correct. He discovers that in fact they are frequently met with ridicule, disrespect and complete rejection by his fellows. As the result of these experiences, he modifies the ideals set before him by his parents and builds up ideals and principles of his own. As he slowly becomes wiser through experience, he builds his own authority and forms his own opinions. He gradually learns to renounce the gratification of obedience to parental authority, and becomes less and less dependent upon it for his inner comfort and satisfaction. But regardless of how old he becomes and the degree of wisdom to which he attains or the extent of his sophistication he never becomes completely mature emotionally. There is no such object in nature as an adult who is completely mature emotionally. The effects of many forgotten admonitions and criticisms in childhood, of prohibited acts, phantasies and thoughts of the immature period may still be present in the unaware consciousness of the adult, influencing thought and conduct and consequently affecting the habit patterns of character. These conditioning influences of childhood are perhaps the only important environmental factors, for the specific way in which the individual reacts to them is due primarily to his particular constitutional make-up, whether he meets criticism and discipline with open and successful rebellion or retires to his corner whipped and assumes the rôle of the overgood child or becomes a nervous, irritable, frightened person depends first upon the degree of sensitiveness with which he was born and his inherent instinctive make-up, and only lastly upon the stimuli arising from the environment.

Therefore the physician cannot be content in unearthing ancient conflicts between conscience and instinct but must discover and help his patient to understand what inherent qualities of his own personality caused him to react to these common difficulties in such a way as to contribute to the formation of a psychoneurosis.

We have said that the treatment of the psychoneuroses consists of three major efforts:

1. To disclose to the patient the original causes of his hypersensitiveness, including those of a basic constitutional nature, if possible.

2. To assist him in the development of insight into the origins, the nature and the function of the maladaptive reactions.

3. To use this understanding of the fundamental qualities of his personality as the foundation upon which to erect a more efficient plan of living in the future.

Studying the patient according to the method suggested in this paper, and with the knowledge gained from physical examinations, laboratory studies and careful survey of the patient's heredity, etc., we are frequently able to find and disclose to the patient his inherent hypersensitiveness and the specific nature that it has acquired. This fulfills item one of the psychotherapeutic program.

In taking the patient through his own growing-up processes by helping him to give the fullest possible history including an account of parental, social, educational, religious and other influences, supplemented if need be by controlled association, we endeavor to find the sources of his difficulties in adaptation, including such overloaded emotional values as may be associated therewith. This should result in the gradual development of insight into the origins of his troubles. As he gains perception he becomes aware of the real nature of his illness, and finally is able to realize that his nervous condition is functioning as a means of defense or escape. Ultimately he becomes aware of the fact that his illness is the result of his own hypersensitive reactions to the circumstances of the environment rather than that the environmental situations are more powerful than his personality and his ability to handle and solve them. This completes the second state of reeducation.

Finally, the third effort in the reeducational process is begun. In this stage the patient uses the knowledge he has gained of the elements which constitute his personality. He has already developed an intimate knowledge of those elements of his personality which have been responsible for causing his neurosis. With the help of the patient and by thinking *with* him in place of thinking *for* him more practical concepts of life are built up and better planes for a balanced life can be formulated.

When the period of intensive reeducation has been completed and there has been some incidental but important practice in the daily application of the principles taught, the patient is discharged and returned to his own environment for a trial trip. Following his discharge, close contact is maintained in order that his progress may be supervised, which is accomplished by one or more return visits of brief duration for review and advice.

TOTAL LEUKOCYTE COUNTS IN HUMAN BLOOD DURING PREGNANCY *

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VIRCHOW spoke of a physiologic leukocytosis of pregnancy, and by the weight of his authority the assumption was given validity, repeated in textbooks, but as far as can be found out, never very seriously investigated. De Lee¹ elaborates the idea by stating that during pregnancy, from the first few months, there is a decrease of the red blood cells and an increase of the white blood cells, the latter out of proportion to the former yet seldom exceeding 15,000; that the younger forms increase so that the blood of pregnancy resembles that in an acute infectious disease, and further that the changes are more marked in primiparae. Williams² mentions a leukocytosis during labor. Cragin³ gives some average counts: during pregnancy 10,600, during labor 12,800, the third and tenth days post partum 11,700 and 10,300. Polak⁴ says that extreme changes are not seen, but that the number of white cells is increased and especially so in the later weeks of pregnancy. Jellett and Madill⁵ repeat what appears in other texts; namely, that there is an increase in the white blood count toward the end of pregnancy. Bland⁶ is a little more specific in that he sets an upper limit at 20,000, and declares that there is invariably an increase. Both of these latter authorities mention that the increase is largely polymorphonuclear and more likely to be marked in primiparae. Piney and Wyard⁷ and Piney⁸ specify a neutrophilic shift to the left, usually without any evidence of infection, and particularly definite in the later months. They assume it to be a physiologic condition. Inasmuch as there have seldom been actual figures given to substantiate these often repeated statements, we determined to establish, if possible, a basis for proof or disproof.

We have gathered together 977 white blood counts from 134 presumably normal pregnancies; 169 pregnancies were studied, but only those cases in which five or more counts were obtained were finally tabulated. Practically all of these women had, either during the period of prenatal observation, post partum, or at some other time contiguous to the pregnancy, a physical examination. They were all considered to be normal women. There were no abnormal conditions during the prenatal period of observation that we thought could in any way affect the leukocytic level. The only infections found were upper respiratory infections in four, Trichomonal vaginitis in four, acute enteritis in one, cervicitis in three, pyelitis in three. Only in the latter might there have been some effect on the white blood

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TABLE I
Leukocyte Counts in Pregnancies during Which Pyelitis Occurred

Mo.	Primip. 1		Primip. 2		Primip. 3	
	W.B.C.	Urine	W.B.C.	Urine	W.B.C.	Urine
II	12,550	pus				
III	15,000	"	9,500	clear		
IV	9,900	clear				
V	13,550	pus	12,050	pus	11,300	clear
VI	14,100	"	12,300	"	14,000	"
					14,850	"
VII	10,100	"			11,850	pus
VIII	10,400	"	12,600	"	12,750	"
					10,100	"
IX	8,900	"	11,950	"	12,000	clear
	9,250	"	11,950	"	10,350	
	10,650	"	8,200	"	12,450	

count (table 1). It will be seen by comparison with the other tables that the increases in these cases are not greater than those often seen in women entirely free of infection (table 2, case 2, for instance).

There were 92 primiparae. There did not seem to be any consistent difference between the level of blood count in these cases compared with that found in multiparae (table 2). A few instances in which the same

TABLE II
Leukocyte Counts in Pregnancy, Comparing Primiparae, Multiparae and Non-Pregnant

Mo.	Primip. 1	Multip. 2	Primip. 3	Primip. 4	Multip. 5	Primip. 6	Primip. 7	Primip. 8	Multip. 9
	Other W.B.C. not pregnant		6,800	18,150† 15,050	8,600	6,550‡ 5,650	6,700	10,000	
II			7,750		16,050	9,050			7,450
III	7,600	10,850	6,350	14,500		8,150		13,450	
IV	10,250	13,200			10,750	8,250		10,000	
V	10,350		9,350	19,400	10,000		7,800	8,500	10,950
								10,450	
VI	7,050	15,650	7,850	17,600		11,850		10,250	
VII	7,950	12,750	8,450	20,650	12,750	12,100	6,150	9,200	13,900
		13,800		18,500				10,250	9,500
VIII	8,650	12,800	6,250	16,100	11,800	12,150	7,700	9,000	11,750
	7,650	13,800	8,600		11,150				9,100
	9,000								
IX	10,150	19,400	9,950	15,800	8,150	9,950	7,300	10,000	7,950
	8,500	15,750	8,650	17,950			6,800		10,800
	8,350	15,000	8,900	18,450			7,800		8,450
	8,050	16,250	8,250						
			7,450						
			7,750						
			8,300*						

* Two days before delivery.

† Acute upper respiratory infection.

‡ One year later—in hospital for gall-bladder operation.

TABLE III
Leukocyte Counts in More Than One Pregnancy in the Same Patients

Mo.	Case 1		Case 2		Case 3		Case 4	
	1st Preg.	2nd Preg.	2nd Preg.	3rd Preg.	1st Preg.	2nd Preg.	1st Preg.	2nd Preg.
II				12,350				
III	10,150					9,200		
IV	11,650	10,400		7,100	6,550		8,900	9,750
V	6,900	13,100	7,800			5,900	7,650	7,900
VI	7,900	8,850		9,400	6,250			10,150
VII	9,850	10,250		8,500	5,750	8,050	9,900	
				8,000			9,900	
VIII	9,400	8,750		9,900		5,900		8,050
		8,100		10,150				8,500
IX	8,950	13,050	10,350	8,150	5,900	8,150		6,450
	7,250		6,800	8,600		8,550		
	8,200		6,700	8,300				
			6 yrs. ago not preg. 7,900					
			4 yrs. ago not preg. 7,800					

woman was observed through two pregnancies, are tabulated (table 3). In a few isolated cases we found in the record white blood counts done when the patient was not pregnant. In some these differed, in others the pregnancy count corresponded very well with the interval count (tables 2 and 3).

All of these counts were done by one technician (H. B.), and most of

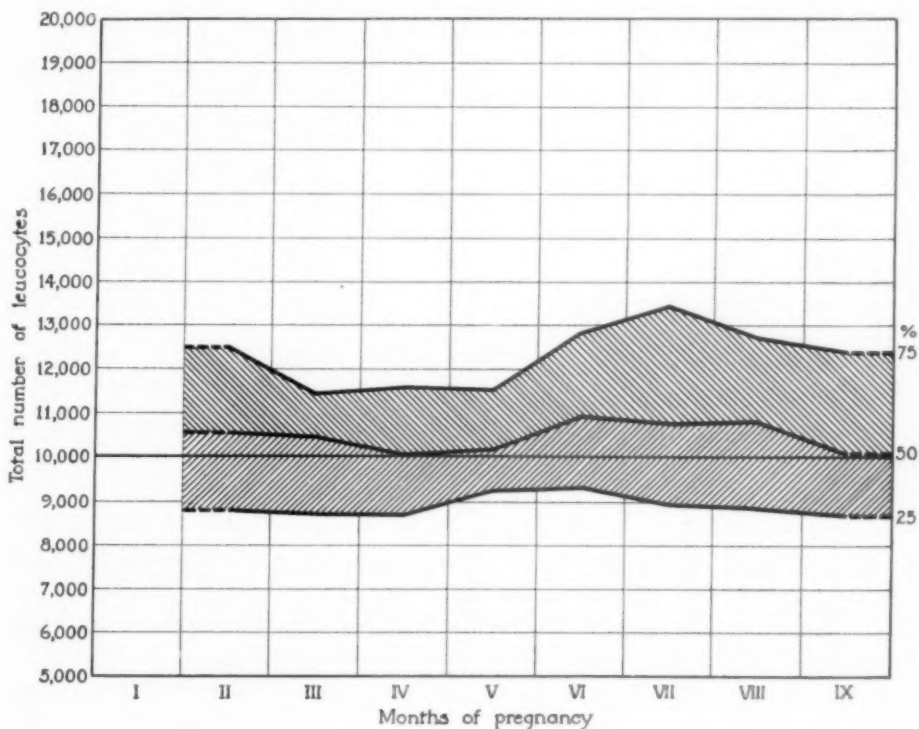


CHART 1.

them were taken in the afternoon, usually later than two hours after the noon meal. A few counts were taken in the morning, usually about three or four hours after a meal. No attempt was made to control any factor which might affect the count, such as exercise, anemia, etc. All of the patients were ambulatory office patients.

We have chosen to chart the median curve, since the counts are not evenly distributed throughout the whole period of gestation, nor for any given month, and such a curve more clearly indicates the center value. The median is the middle case, so that 50 per cent of all counts are above and 50 per cent below. We have also charted the percentile lines, establishing the four quartile zones of variation. Lacking values of normal for non-pregnant women, we have assumed 10,000 to be the probable upper limit of normal, since counts higher than this are commonly considered pathological by most clinicians (chart 1).

There were in general three types of curves seen in a study of individual cases: one a curve that approximated the median one charted (table 2, cases 1, 5, and 6); another which remained throughout on a high level (table 2, cases 2, 4, and 8); and a third which remained throughout on a level well within normal limits (table 2, cases 3 and 7). It is apparent from the charted curves of median and percentile values, and also in the individual cases cited, that there is no consistent rise in the ninth month, also that less than 50 per cent of the counts are below 10,000. The impression is that some women respond with a leukocytosis to pregnancy and others do not.

There was nothing unusual in the cell morphology of those cases showing an elevation of the white count. The elevation seemed to be predominantly of the neutrophilic cells.

SUMMARY

1. Nine hundred and seventy-seven leukocyte counts in 134 normal pregnancies were obtained.

2. A count between 10,000 and 11,000 seems to be a median value for pregnancy, irrespective of time in pregnancy.

3. Fifty per cent of the counts were between approximately 8,700 and 12,500 throughout the nine months of pregnancy.

4. Less than 50 per cent of the counts were below a high normal of 10,000.

5. Seventy-five per cent of the counts were above 8,700.

6. Twenty-five per cent of the counts were above 12,500 or below 8,700.

7. There was no rise in the ninth month, except in a few individual cases which were not numerous enough to lift the curve.

8. Some patients remained consistently high throughout the nine months; others remained consistently low or normal.

9. There did not seem to be any significant difference between curves of counts in primiparae and multiparae.

10. There may be a physiologic leukocytosis of pregnancy, but it certainly is not invariable.

We are indebted to Dr. Edith Boyd for her help in preparing chart 1.

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THE CONTINUOUS METHOD OF TREATMENT OF EARLY SYPHILIS *

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If early syphilis is properly treated, late syphilis will almost, even if not quite, disappear. That early syphilis is not being properly treated is obvious from the fact that late syphilis is not disappearing. On the contrary, in every urban American community syphilis heads the list of reportable communicable diseases, and of the cases reported, more than half are late cases.¹

The proper treatment of early syphilis is of importance from three standpoints: that of the individual patient; that of the public health; and that of the public expense. The individual patient requires proper treatment in order to accomplish "cure" and to prevent the development of usually serious, often crippling and disabling, and sometimes fatal late lesions. To utilize the two most serious of these, cardiovascular and neurosyphilis, as an



FIG. 1.

* Presented at the Detroit meeting of the American College of Physicians, March 3, 1936.

From the Syphilis Division of the Medical Clinic, the Johns Hopkins Hospital.

illustration figure 1 shows the approximate incidence of each in patients untreated or badly treated as compared with those given adequate early treatment. Similar data are available for all the late sequelae of the infection.²

From the standpoint of the public health, the spread of syphilitic infection may best be controlled by the elimination of the infectious patient.

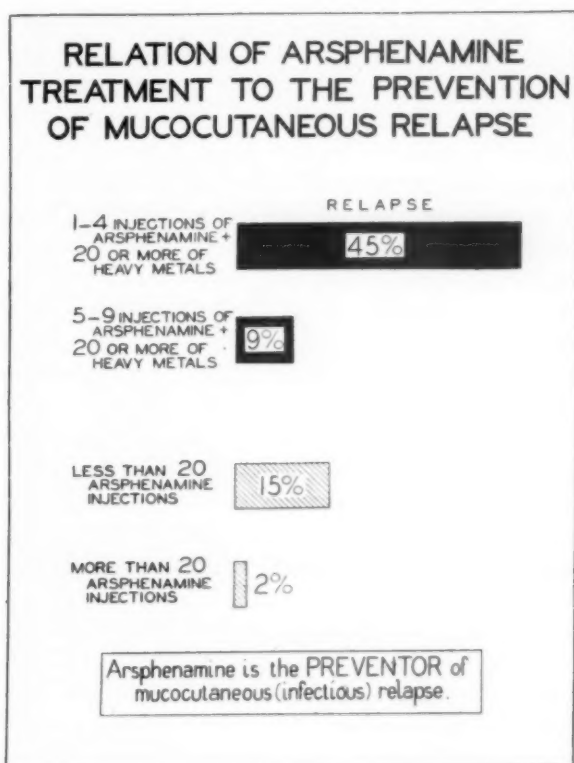


FIG. 2.

Figure 2 * shows that (1) an arsphenamine is necessary to prevent infectious relapse—heavy metal alone does not suffice; (2) less than four injections of an arsphenamine permits relapse in the astonishingly high total of 45 per cent, an incidence probably even higher than would occur if no treatment were given (though data on this form of relapse in untreated syphilis are lacking); (3) at least 20 injections of an arsphenamine are the absolute

* All figures except figures 1 and 10 are based on the data of the Coöperative Clinical Group (the Syphilis Clinics of the Universities of Pennsylvania, Michigan, Western Reserve, Johns Hopkins University, and the Mayo Clinic). The papers on which these charts are based are listed in the bibliography as reference 3.

Figures 2, 7, 8, and 9 have been prepared by the American Social Hygiene Association and are here published for the first time with permission. These and 19 other similar figures illustrating the studies of the Coöperative Clinical Group on early and latent syphilis are available in pamphlet form (price 30 cents) from the American Social Hygiene Association, 50 West 50th Street, New York.

minimum required nearly to eliminate infectious relapse. The practical abolition of infectious relapse is related not only to the total amount of treatment given, but also, as will be shown, to its type. It is important here to emphasize, however, that the public health aim of treatment, and the end sought in the individual patient, require a type and total amount of treatment not very different for the one than for the other.

The economic aspect of the proper treatment of early syphilis is of fundamental importance. Hospital beds, both general and psychiatric, are filled with patients who must be treated and maintained at public expense, who are no longer a menace to the public health since they are no longer infectious, and whose prospect of "cure" or even of symptomatic relief is, as compared with early syphilis, negligible. In Baltimore, the annual expense of hospital care for such patients, for the average year (determined in 1933) is \$100,000.⁴ If this sum is expended in one city of not quite a million people, it is a fair estimate that the hospitalization of broken down late syphilitics (whose illness is nearly irremediable) in the country at large costs approximately \$12,400,000 annually. The amount of money expended by Health Departments and privately endowed hospitals on the ambulatory care of patients with early syphilis, i.e., at a time when "cure" can be accomplished and the development of late sequelae requiring hospitalization prevented, cannot be so readily estimated but is probably nowhere nearly so large a sum. It seems logical to conclude that the expenditure of money is being made in the wrong place; and that by increasing greatly the amount spent on the proper care of early syphilis, the ultimate cost of late syphilis could be greatly reduced.

If one grants that, by and large, early syphilis is not being properly treated, it is wise to enquire into the reasons for this difficulty. The fault seems to lie in part with the biology of syphilitic infection, in part with the laity, and in part with physicians.

It is now quite clear that in some patients, perhaps in many, who are infected with syphilis, the lesions of primary and secondary syphilis are either wholly absent or so trivial and transitory as not to attract the attention of even the most observant individual. Infection has been, for all practical purposes, symptomless. If a patient does not recognize symptoms serious enough to take him to the physician at all, obviously he cannot be treated. Such patients form an as yet unmeasured reservoir for the spread of infection to others, and for the ultimate development of late syphilis. The physician has only one defense against this biologic silence of syphilitic infection, namely the use of the routine serologic test for syphilis on every possible occasion. Case finding is as important in syphilis as it is in tuberculosis.

The fault which lies with the laity is ignorance, and worse still, unwillingness to learn. Many individuals, perhaps most, know little or nothing of syphilis—its symptoms, its late complications, its prevalence. Most persons know only that the disease is "venereal" and usually contracted through sexual intercourse. The sex taboo forms the barrier to the acqui-

sition of accurate knowledge. There is a "conspiracy of silence" concerning syphilis. The press, daily and periodical, and the radio, too often bar even the mere mention of the word, let alone informative discussion concerning it. The public must be educated to know what syphilis is, and trained to consult a physician for its earliest symptoms as it has been similarly trained for tuberculosis and cancer. The dangers of quack, drug store, or self treatment must be pointed out. Until the patient knows enough about his possible illness to consult a physician for it, the hope of getting him under early treatment is an idle one. Until he knows something of the requirements of proper treatment, and the possible consequences of evading it, it is useless to expect his cooperation in carrying it out.

The fault of the medical profession is threefold: that it has not taken the lead in education of the laity; that it does not apply modern methods to early diagnosis; and that, though adequate treatment methods have been developed, it does not apply them. Further discussion of the educational aspects of the problem are beyond the scope of this paper. It is essential to point out, however, that the reasons for the failure to control the syphilis problem are not wholly due to the inadequacy of current modern treatment.

To concentrate now on the question of treatment, it is readily apparent that the failure of physicians as a group is due in small part to technical ineptitude, and in large part to the persistence of empiricism. There are a few simple principles applicable to the treatment of early syphilis, all of which are backed by sound experimental and clinical evidence. These are:

- (1) Successful treatment depends on early diagnosis.
- (2) The choice of drugs is limited to the arsenicals represented in the arsphenamine group, and to bismuth.
- (3) Treatment should be continuous from start to finish, i.e., without rest periods of any sort.
- (4) Treatment must be prolonged to a minimum of (depending on the stage of infection) 12 to 18 months.
- (5) Determination of "cure" requires life long post-treatment observation.

The importance of early diagnosis is shown in figure 3. The patients on whom this chart is based were treated by several different methods and in varying amounts—not with the best method and for the optimum time. Even with this handicap seronegative primary syphilis is 72 per cent "curable"; whereas the prospect of "cure" drops by 20 per cent with the few days' or weeks' delay necessary for the development of a positive serologic test or secondary lesions. To increase the probability of early diagnosis of seronegative primary syphilis, it is essential (1) to educate the layman to consult a competent physician at once on the appearance of any genital sore; (2) to educate the physician to use the dark field microscope or to refer his patient to some one who can.

The choice of drugs is limited to the arsenicals represented in the arsphen-

amine series, and to bismuth. This point should not require elaboration. No other arsenical drug is known which is of comparable value to the arsphenamines in early syphilis, though one still sees patients treated with

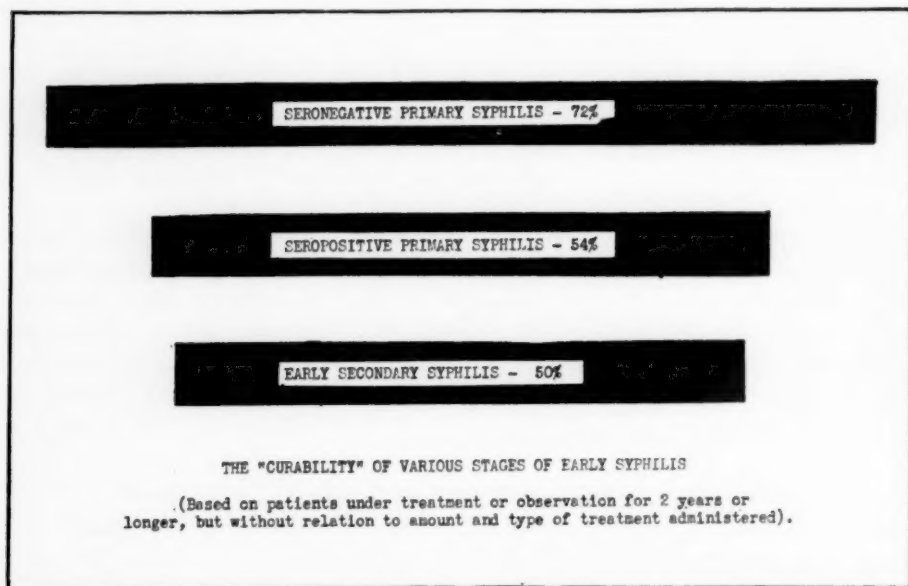


FIG. 3.

pentavalent arsenicals (useful only in neurosyphilis), with sodium cacodylate, or with bizarre and untried arsenicals boosted by pharmaceutical houses. Among the arsphenamines, only arsphenamine itself (606), neoarsphenamine (914), silver arsphenamine, and mapharsen (arsenoxide) are worthy of serious mention; and in spite of the 25 years of study devoted to the subject, a serious comparison as to the relative merits of these four is available only for arsphenamine and neoarsphenamine (mapharsen has been too recently introduced for comparative data to be evaluated). As between 606 and 914, however, the advantage is definitely with arsphenamine. Figure 4 shows that the prospects of "cure" are 16 per cent greater, and the prospects of clinical relapse 5 per cent less with arsphenamine than with neoarsphenamine. This variation seems to be too slight to persuade the average physician to use the technically difficult arsphenamine in place of the technically easy neoarsphenamine. Fortunately, however, it is probably true that arsphenamine results can be approximated with neoarsphenamine if larger doses and longer courses of the latter are given to compensate for its therapeutic inferiority. As a matter of fact, it is probable that satisfactory results may be obtained with any of the four arsphenamines mentioned, if they are given in adequate dosage by the continuous system and for a long enough time.

As between bismuth and mercury, the advantage is definitely with bismuth, as is shown in figure 5. Where arsphenamine plus bismuth is given serologic reversal is 12 per cent more frequent, and infectious relapse 6 per

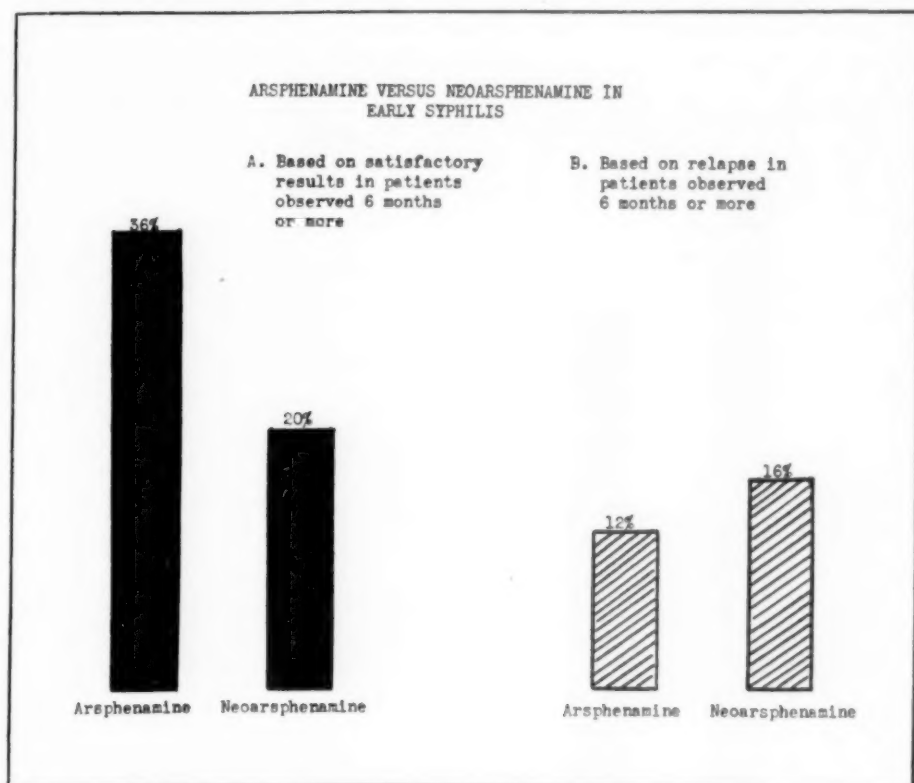


FIG. 4.

cent less frequent, than if the same amount of arsphenamine plus mercury is used. The bismuth preparation employed should not be, for reasons beyond the scope of this paper, water soluble; but should be liposoluble or an insoluble salt suspended in oil.

Treatment should be continuous. The reasoning which led to the adoption of this method of treatment is briefly as follows, and is based on the interplay of the biology of syphilitic infection, the mechanism of drug action, and the phenomenon of drug resistance.⁵

Early syphilis may occasionally be "cured" by one or a few injections of an arsphenamine, with or without associated heavy metal. In the majority of patients, however, biologic "cure" does not result from a small amount of treatment. Treatment, whether adequate or inadequate, interrupts the development of resistance (or immunity) to the virus, and may actually depress it, by preventing the normal sequence of events in an un-

treated patient, i.e., gradually developing insusceptibility to reinfection, spontaneous healing of secondary lesions, spontaneous destruction of treponemes, and latency. If treatment is inadequate (or intermittent), and the patient is left, at the beginning of the first rest period, with living treponemes in his tissues, he must elaborate his immune reactions afresh against these remaining organisms. Depending on the location of the surviving organ-

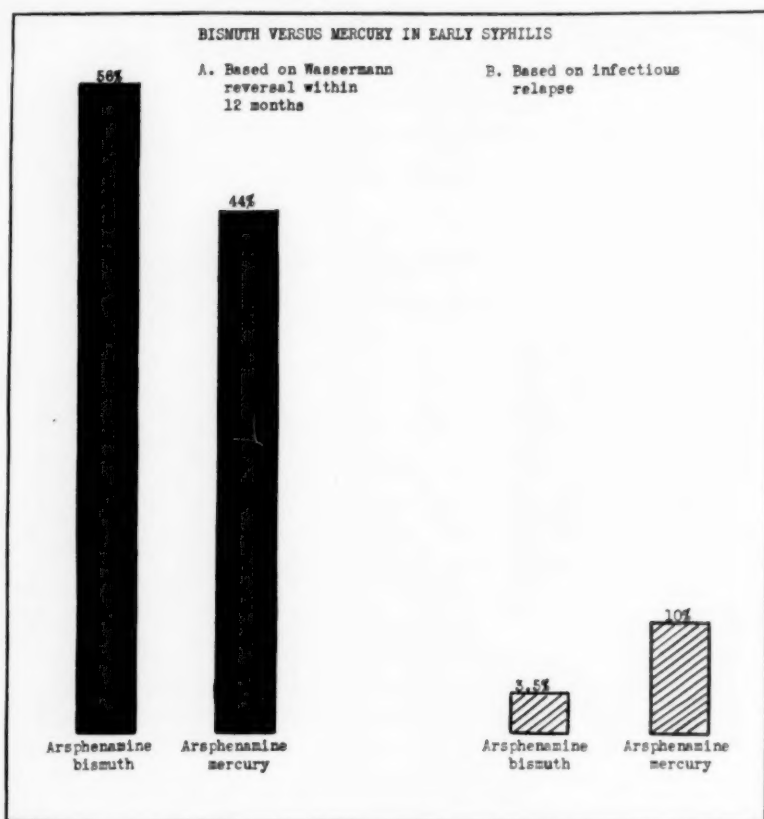


FIG. 5.

isms and the interval between treatment courses, he may not develop obvious clinical or serologic evidence of relapse, though some degree of biologic relapse may be expected unless the amount of treatment before the rest period has been adequate to destroy every treponeme.

If treatment is purposely intermittent, combining an arsphenamine and a heavy metal in a single course, rest periods are obligatory because (1) the patient's tolerance to toxic drugs must not be exceeded; (2) experimental and clinical evidence indicates that sometimes, if not always, the organisms acquire a tolerance for the drugs employed, and become drug resistant. Under these circumstances, the obligatory rest period, leaving the patient

without the protection either of chemotherapeutic treatment or of his own defense mechanism, paves the way for relapse.

With continuous treatment, on the contrary, courses of an arsphenamine may be given in alternation with courses of a heavy metal, without rest periods of any sort. Under these circumstances, the patient's tolerance for

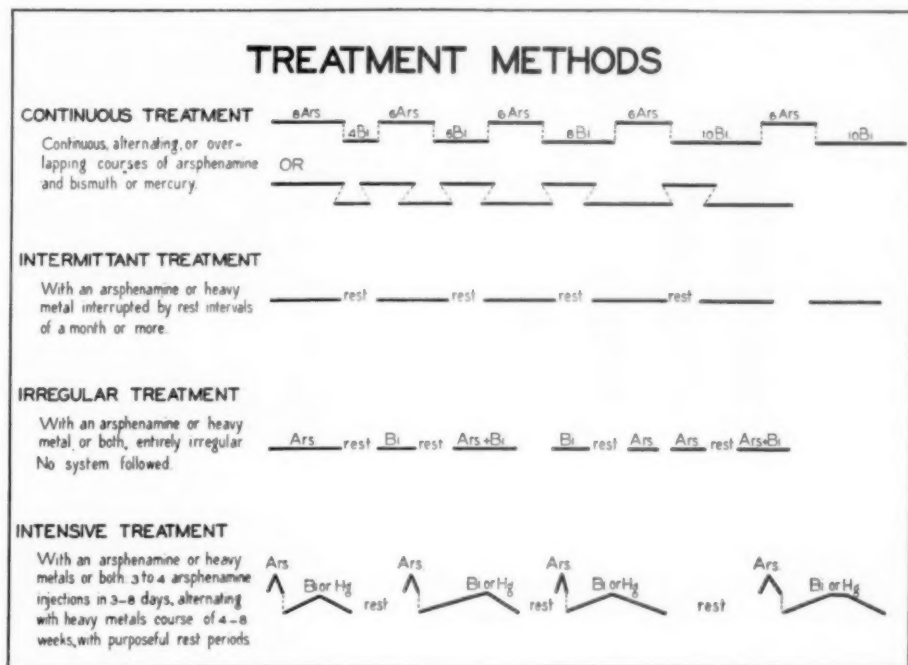


FIG. 6.

toxic drugs need not be exceeded; the phenomenon of drug resistant strains of organisms need not be feared (since drug resistance is usually drug specific); and most important of all, the patient's own defense mechanism is constantly augmented or replaced by the continuous effect of treponemicidal, treponemistatic, or resistance-building drugs.

The test of this reasoning is, of course, the results obtainable in human beings by the use of the method. Moore and Kemp,⁶ in 1926, presented data showing the superior results of continuous over intermittent treatment; and their findings have been confirmed on a much larger scale by the Co-operative Clinical Group and by the League of Nations enquiry into syphilitic treatment. From all points of view studied, both major and minor, the treatment of early syphilis is more successful with the continuous than with any other method. Here it is necessary only to discuss briefly three of the most important points: (1) the ultimate clinical outcome, i.e., the probability of "cure"; (2) the incidence of clinical relapse; and (3) serologic reversal.

The Coöperative Clinical Group studied the results of four methods of treatment, diagrammed and explained in figure 6. The continuous method accounts for 14 per cent more "cures" in all types of early syphilis and for

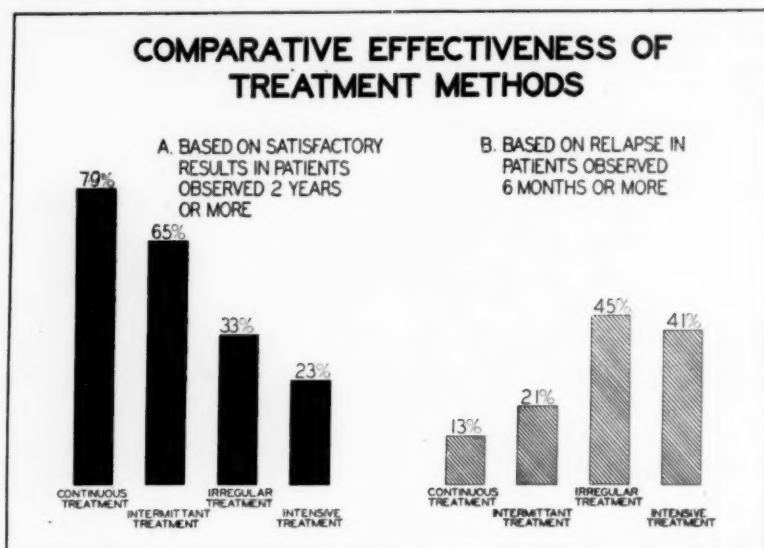


FIG. 7.

8 per cent less relapses, than its nearest competitor, intermittent treatment. Interestingly enough, the intensive (Pollitzer) system gave the poorest results of all, even worse than those of the most haphazard and irregular

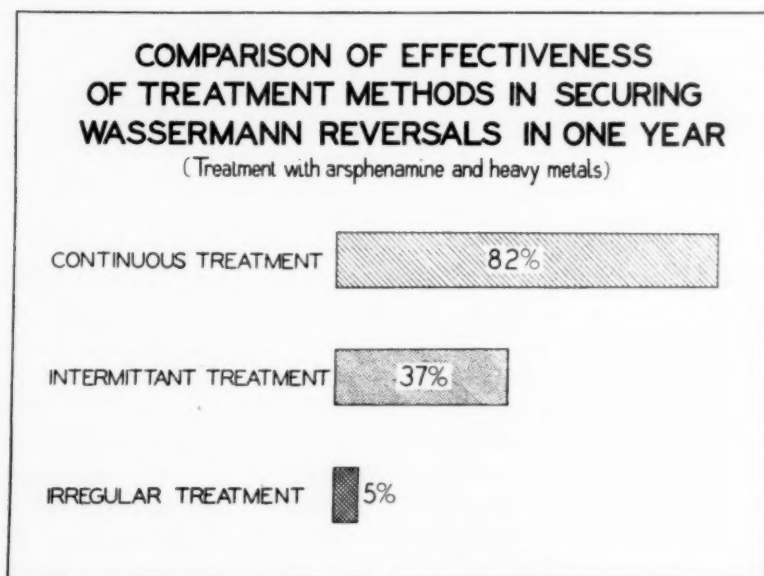


FIG. 8.

treatment (figure 7), a point of considerable interest in view of the revival of a modification of this idea by Chargin and his associates.

The difference between the various treatment schemes in bringing about serologic reversal within a given period of time is even more striking. In figure 8 it is shown that serologic negativity was achieved within a year in 82 per cent of those treated continuously, in less than half as many when treatment was intermittent, and in only 5 per cent of those treated irregularly. The converse of this chart is the obvious fact that in early syphilis, a faulty treatment method may actually be responsible for that feature of

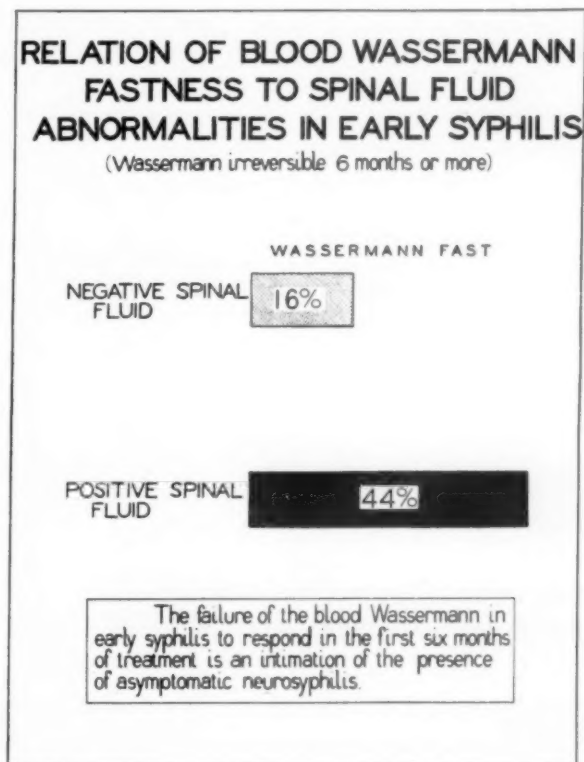


FIG. 9.

syphilotherapy which most disturbs the average physician, namely, Wassermann fastness.

More serious still, intermittent or irregular treatment causes an increased incidence of serologic evidence of invasion of the nervous system, i.e., asymptomatic neurosyphilis. Fortunately for the patient, though not generally appreciated by the therapist, there is a close relationship between the incidence of these two factors, asymptomatic neurosyphilis and Wassermann fastness (figure 9). If in early syphilis (not true of late syphilis) the blood serologic test remains persistently positive for six months or longer, the

cerebrospinal fluid is nearly three times as likely to show evidence of neuraxis invasion as when serologic reversal has occurred. A persistently positive blood test in treated early syphilis urgently demands routine spinal fluid study. If asymptomatic neurosyphilis is present, intensification or modification of the routine treatment scheme is required.

Treatment must be prolonged to a minimum (depending on the stage of infection) of 12 to 18 months. While it is true that some patients are "cured" with much less treatment than this, there is no way in which such fortunate individuals may be recognized before or during treatment. It is essential, therefore, to give all patients enough treatment to "cure" the most resistant member of the group, even though this amount is more than some may need. The minimum duration of treatment has been arrived at on the basis of prolonged experience under rigid serologic and clinical control. The essential data justifying the standard named are presented in figure 10, which shows the approximate probability of "cure" with varying

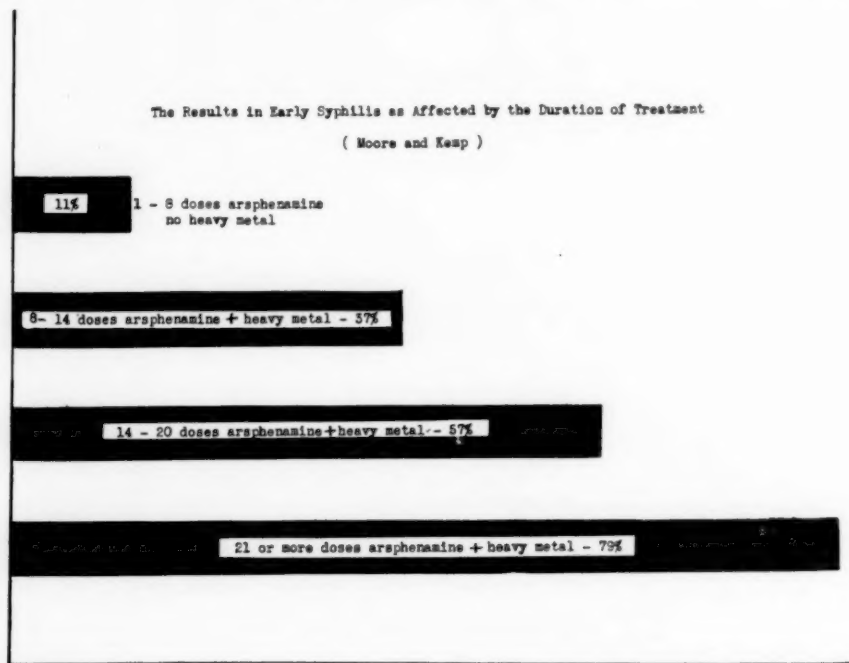


FIG. 10.

amounts of treatment. It must be remembered that these data are applicable only to patients with uncomplicated early syphilis, in whom the course of the disease and of treatment has been uneventful. Patients with clinical or serologic relapse, with treatment resistance, with grave treatment reactions which interfere with subsequent intensive treatment, and with asymptomatic neurosyphilis, are not included. For such persons, treatment is a

highly individualized procedure, usually demanding expert consultative advice.

The optimum duration of treatment is slightly shorter if the diagnosis is made and treatment started during the seronegative primary stage, when, given a coöperative patient and no complications, "cure" is nearly certain with 12 months of continuous treatment. With seropositive primary and early secondary syphilis, 18 months of treatment are required to produce results which are not quite so certain.

The duration of treatment may be measured if desired, though preferably only by the expert, by serologic standards. On this basis, the criterion set by Keidel 20 years ago still holds good, namely, one full year of continuous treatment after serologic tests of blood and cerebrospinal fluid have become and have remained completely negative. Since the use of such a standard demands frequent repetition of serologic tests, thereby adding to the cost of treatment, and since difficulties of interpretation of such serial serologic testing confront both the inexperienced physician and his anxious patient, it is probably better for the average practitioner to discard the serologic method of treatment control and to rely on the arbitrary standard already mentioned. These standards, i.e., 12 months of continuous treatment for seronegative primary syphilis and 18 months of continuous treatment for seropositive primary or early secondary syphilis, are in fact based upon the correlation of clinical and serologic standards in thousands of patients treated under expert control.

Determination of "cure" requires lifelong post-treatment observation. There is no other criterion of "cure" in human beings. Until quite recent years it was the custom even for the expert to dismiss his well treated patient as "cured" within 1 to 3 years after the completion of treatment; and this brief observation period is still the custom of the less experienced physician. Brief thought as to the extreme chronicity of syphilis in untreated, or if treated in uncured, patients shows the advisability of prolonged follow-up. Fifteen to 20 years after infection usually elapse before the development of obvious signs of the two important late sequelae, cardiovascular and neurosyphilis. To protect one's treated patient against such disasters, a year or two of casual post-treatment observation is not enough; the patient must be followed for a life time. The treated syphilitic patient is the ideal subject for the periodic health examination.

SUMMARY

Though the adequate treatment of early syphilis is of importance from the standpoints of the individual patient, of the public health, and of the public expense, and though proved adequate treatment methods are available, they are not being generally applied.

The reason for this failure lies in part in the biology of syphilitic infection, i.e., in the fact that it is sometimes, perhaps often, symptomless in

the early stages; in part in lack of knowledge of the laity of the prevalence, characteristics, and public and individual importance of syphilitic infection; in part in the failure of the medical profession to employ adequate methods of early diagnosis and treatment. Remedies for these three faults are briefly suggested.

The modern treatment of early syphilis is based on five fundamental principles, as follows:

- (1) Early diagnosis.
- (2) The use of drugs of proved worth.
- (3) The use of a continuous treatment system, without rest periods.
- (4) The use of treatment prolonged to an arbitrary minimum of 12 to 18 months.
- (5) Determination of "cure" by lifelong post-treatment observation.

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GLANDERS *

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GLANDERS, although an uncommon disease in man, is so frequently misdiagnosed, so pernicious in its manifestations and of such great importance as a public health problem when it does occur that it merits more attention than it has so far received. There are but few states that provide, in their public health laws, for the protection of their residents against this disease. Since the advent of the motor car, glanders in man has materially decreased, but in rural districts and especially in the southwestern states many cases probably go undiagnosed and constitute a genuine danger to the public health.

Strictly speaking the term glanders should be limited to the infection of the nasal mucous membrane and the internal organs, while the term farcy designates the skin and lymphatic manifestations of the same disease. In general terms glanders may be defined as a specific infectious disease due to the *Bacillus mallei*,† not uncommon in the horse, mule and ass and contracted by man through immediate contact with an infected animal.

Glanders may be either acute or chronic. The acute type is very frequently devastating in the rapidity of its evolution and often takes the form of a septic pneumonia secondary to a primary nasal mucous membrane infection. It is often mistaken for general sepsis, the nature of the primary lesion passing unrecognized. The acute cases are usually fatal and from a public health point of view not as important as the chronic type.

Chronic glanders presents no characteristic symptomatology. The essential lesion is an infectious granuloma that breaks down, as a rule, rather rapidly with the formation of slow healing ulcers in the skin and mucous membranes and deep seated abscesses in internal organs, muscles and other parts of the body. Bone infections have been noted. In cases where the virulence of the infecting organism is low, there is considerable epithelioid cell formation and also giant cell production. This type of lesion is not unlike a tubercle. These patients present symptoms of a chronic septic character with intervals of remission that may be short or long. A very few recover, the majority succumb to an acute exacerbation usually with acute pulmonary manifestations.

The two cases I have to report are of the chronic insidious type with no initial acute manifestations. The first case was under observation but a short time, while the second one has been observed for over five years.

* Received for publication June 1, 1935.

† *Actinobacillus mallei*.

CASE REPORTS

Case 1. A white female, aged 36. Her previous history is irrelevant except that she was reared on a farm and that she came into intimate contact with two horses that died of an unknown disease 18 months previous to her present examination. Shortly after the death of the above mentioned horses she first noticed a slight nasal discharge followed shortly by the formation of an ulcerated patch on the tip of the nose. The nasal discharge gradually increased and became mucopurulent, while the skin lesions advanced until the entire upper lip and nose presented an ulcerated, discharging mass. She consulted a number of physicians and the diagnosis varied from syphilis and tuberculosis to epithelioma. At no time did she suffer from marked constitutional symptoms. At the time of examination the patient was well nourished and the physical examination revealed no abnormalities except as portrayed in figure 1.



FIG. 1. The glanders lesions of the nose and lip in case 1.

The temperature, blood count and urine examination were all normal. The blood Wassermann was negative. Tests for the tubercle bacillus were negative and tissue examination revealed no malignancy. (Figure 2.) There were no laryngeal symptoms. The skin lesions were covered with a thick, yellowish crust which after removal revealed many small ulcerations on a surface of granulating tissue. Smears from the discharge from the nose and from the skin ulcerations revealed a mixed infection with many gram-negative, slightly curved rods. This organism proved to be *Bacillus mallei*, and the patient's blood agglutinated a known organism in dilutions up to 1-160. Treatment with an autogenous vaccine, together with such local treatment as was indicated, was instituted, but the patient refused to remain under my care and the eventual outcome in this case is not known.

Case 2. A Mexican youth, aged 15, presented himself for treatment because of the loss of sight in one eye, a severe infection in the other eye, a mucopurulent discharge from the nose and extensive ulceration of the nose and upper lip as shown in figure 3.

His previous history was irrelevant except that he had come into intimate contact with a horse that had died from some unknown disease shortly before he became ill. The patient stated that the disease manifested itself first by a redness and discharge from the lower lid of the left eye. One and one-half years later this was followed by a discharge from the nose and ulcerations of the tip of the nose that gradually spread to the upper lip. He next noticed some slight hoarseness and difficulty in swallowing. About six months previous to his present examination (July 1929), his right eye became infected. At no time did he suffer any constitutional

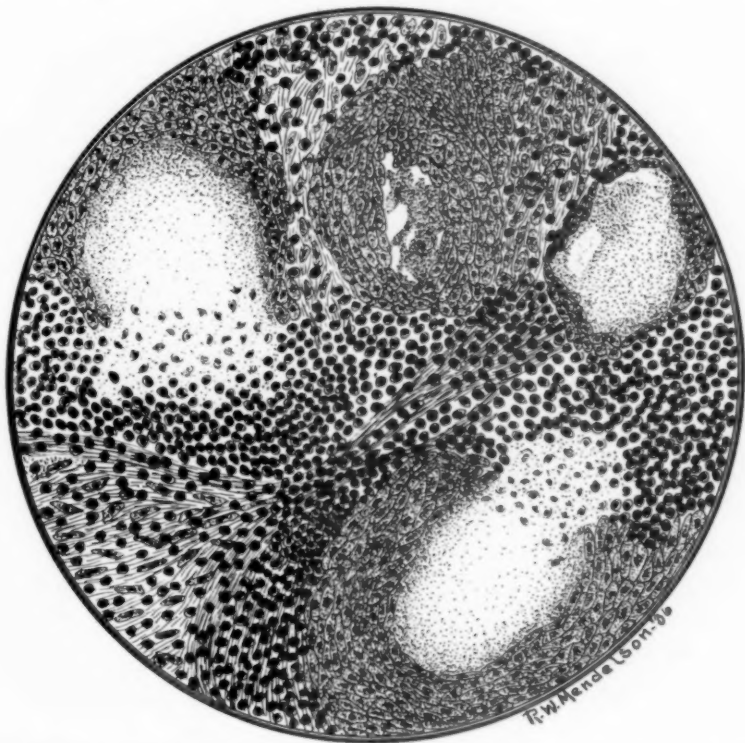


FIG. 2. Section from case 1, showing granulomas made up of masses of epithelioid cells with central necrosis. There is abundant leukocytic infiltration. No giant cells are to be seen in this section.

symptoms. On physical examination he presented an emaciated body, considerable enlargement of all of the glands in the neck, a normal blood count, a negative Wassermann and a normal urine examination. The right eye showed considerable corneal ulceration with a high degree of conjunctival inflammation. The left eye presented old corneal ulcers, moderate conjunctival inflammation and considerable mucopurulent discharge. There were no ulcers in the oral cavity, the membranes were injected and there was a well marked nasopharyngeal discharge. The external nasal passages were blocked with encrusted, yellowish deposit. (Figure 3.) The skin lesions were covered with a thick, encrusted mass of discharge that involved the

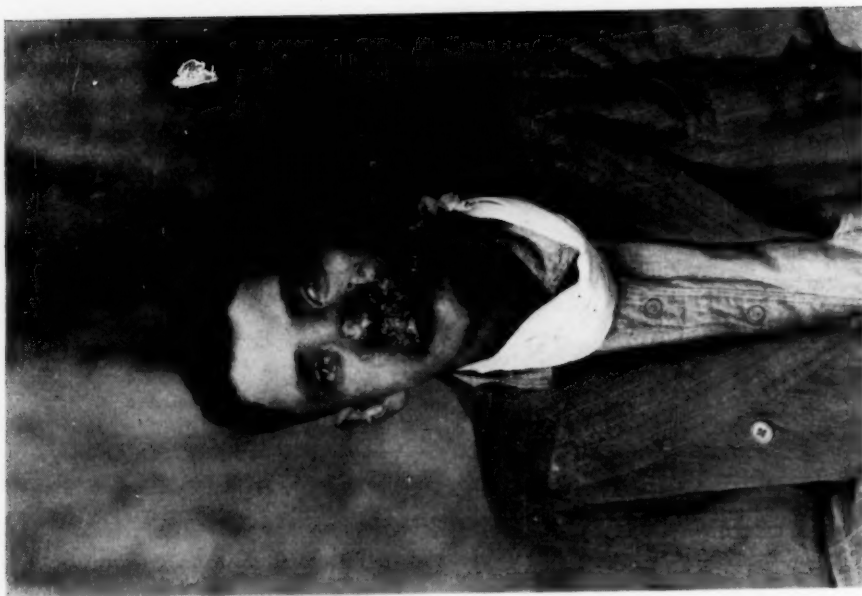


FIG. 3. Case 2, before treatment.



FIG. 4. Case 2, six months after treatment with autogenous vaccine.

mucous membrane of the upper lip to the gum line. Removal of the crusts revealed an ulcerating, granulomatous tissue from which was obtained a mixed infection with many gram-negative, slightly curved rods that proved to be *Bacillus mallei*. This patient's blood agglutinated a known culture in a dilution of 1-160. Treatment of this case consisted of various local treatments and autogenous vaccine. The condition of



FIG. 5. Case 2, three years after vaccine treatment.

the patient six months after treatment is well defined in the illustration (figure 4). After this period of treatment the patient left my service and I did not see him for a period of about two years when he returned and his condition at that time is well portrayed (figure 5). He also has developed in the meantime a large ulceration on the left elbow from which *B. mallei* can be recovered.

COMMENT

The diagnosis in these cases is of course suggested by the history, the characteristic nasal discharge and the ulcerations. Differential diagnosis must take into consideration epithelioma, syphilis and tuberculosis. In the tropics one must also consider the possibilities of a framboesial infection.

These diseases are not difficult to eliminate. Agglutination tests are of primary importance in confirming the diagnosis, and one may either agglutinate the patient's serum against a known organism or, having isolated the specific organism from the patient's lesions, agglutinate it against a known serum.

Regarding the treatment one must not be too optimistic. Apparent cure is often followed by relapse and not infrequently a case will subside without the benefit of medication. Watson of Canada reports good results with the use of hyperimmune serum, but this is difficult to obtain. Autogenous vaccine with indicated local treatment has been my choice, and in view of the tendency to relapse in spite of apparent cure it is advisable to keep these patients under observation for many years. They are at all times a danger to the public health during the active stages of the disease and should be under strict quarantine. While enjoying periods of inactivity they should report at frequent intervals for observation.

THE LOCALIZATION OF SUPRATENTORIAL TUMORS OF THE BRAIN BY OLFACTORY TESTS *

By CHARLES A. ELSBERG, M.D., *New York, N. Y.*

IN a series of papers published in the Bulletin of the Neurological Institute of New York (1935, 1936) new quantitative procedures for the examination of the olfactory sense were described. One of the procedures was called *blast injection of odors* and consists of the injection of measured volumes of odor into one or both nasal passages during short periods of voluntary cessation of breathing. In this procedure the pressure under which the blast of odor is released into the nose takes the place of the force of the ordinary inspiratory movement.

The smallest number of cubic centimeters of an odor that can normally be identified by the blast injection test was called the M.I.O. (minimum identifiable odor) of the odorous substance. The M.I.O. of any one substance was found to have about the same value in all normal individuals.

A second method was called *stream injection of odors*. In this procedure a continuous stream of odor is injected into one or both nasal passages for a period during which the individual who is being examined breathes through the mouth. The stream injection of odors was used to produce olfactory fatigue and to study the trigeminal effects of odors. Here again it was found that the duration of olfactory fatigue for any odor produced by stimulation of the olfactory receptors was about the same in all normal individuals. The effects of blast injection and stream injection of a variety of odors were investigated in a large series of healthy individuals, and information was gained regarding the nature of the olfactory stimulus, the relative importance of pressure and volume of the olfactory stimulus for the olfactory impulse, the physiological aspects of monorhinal, birhinal and bisynchronorhinal smell, and the nature of and organic basis for olfactory fatigue.

Finally two odorous substances—coffee and citral—were selected for clinical tests of the sense of smell. These two substances were chosen because their odors are familiar, and because the odor of one of them—coffee—is a pure olfactory stimulant, while that of citral affects both the olfactory and the trigeminal nerves. Several years were spent in the study of the sense of smell in normal individuals. Finally, in order to learn whether the methods were of value for the localization of tumors of the brain, the tests were used in patients in whom an intracranial neoplasm was suspected.

Up to the present time, we have examined 118 patients in whom an intracranial growth was suspected or considered a possibility. In 52 of the cases,

* Read by invitation at the meeting of the American College of Physicians, Detroit, Michigan, March 2, 1936.

the situation of a neoplasm was verified by operation, autopsy or by pneumography. These 52 cases form the basis for this report.

In order that the reader can appreciate the results and the significance of the tests, it is necessary to give a short description of the procedures called *blast injection* and *stream injection of odors*. The apparatus and methods have been described in detail in other publications.

For our present purpose it will suffice to explain that after the M.I.O. of each side of the nose had been determined, the duration of olfactory fatigue produced by the stream injection of the odors for 30 seconds at a volume-rate of 2000 c.c. to the minute was established for each side of the nose.

The presence of gross abnormalities in the nasal passages was first excluded by the Zwaardemaker test. Then blast injections of the odor of coffee were given into one nasal passage at intervals of 30 seconds until the smallest volume of odor that could be identified at three successive blast injections was determined. After the value of M.I.O. of one side had been found and the patient had been given a few minutes of rest, the M.I.O. of the other side was determined by blast injections. Then, again after a few minutes of rest, the patient was given a stream injection of coffee odor into the nasal passage that had been tested first. The duration of the ensuing olfactory fatigue was established by giving, every 30 seconds, blast injections of the volume that had been necessary for M.I.O., until the ability to identify the odor as coffee had returned. After another rest period, the procedure was repeated on the other side of the nose. Later, similar blast injection and stream injection tests were made with citral. By these procedures the M.I.O. and the duration of olfactory fatigue on each side for coffee and for citral were established.

TABLE I
The Determination of M.I.O. for Coffee in Case 1
Blast injections of coffee odor given every 30 seconds into:

Right Side (c.c.)	Left Side (c.c.)
8 - + *	8 - +
8 - 0	8 - +
8 - 0	8 - +
9 - 0	7 - +
9 - 0	7 - +
11 - 0	7 - +
13 - 0	6 - +
15 - 0	6 - 0
15 - 0	6 - 0
16 - 0	7 - +
17 - +	7 - + = M.I.O.
17 - +	
17 - +	
16 - 0	
16 - 0	
17 - + = M.I.O.	

* + = odor identified; 0 = odor not identified.

The number of blast injections required in a patient before the M.I.O. for coffee of each nasal passage had been obtained is shown in table 1. The table illustrates the steps of the procedure by which M.I.O. is established.

Table 1 shows that on the right side 17 c.c. were the smallest number of c.c. that were identified on three successive blast injections into the right nasal passage, and 17 was therefore the M.I.O. on the right side. Similarly 7 was the M.I.O. on the left side.

Sometimes, as in the instance above given, the M.I.O. can be established by a relatively small number of blast injection tests; at other times a larger number of blast injections has to be given before the examiner is certain that he has obtained the correct values for the M.I.O. Because the injections of volumes of odor corresponding to M.I.O. are used in order to determine the duration of olfactory fatigue, it is important that in the preliminary blast injection tests the volume necessary for M.I.O. be accurately determined.

THE CHARACTER OF THE CHANGES FOUND BY THE OLFACTORY TESTS AND THEIR SIGNIFICANCE FOR LOCALIZATION OF THE GROWTH

In order that the significance of the figures obtained in patients with tumors of the brain may be appreciated, a table of the results of tests in a few healthy individuals is given (table 2). In this table the duration of fatigue is the number of minutes which elapsed after a stream injection of the odor for 30 seconds at a volume-rate of 2000 c.c. per minute, before the odor was again identified.

TABLE II
The Normal M.I.O. and the Duration of Fatigue in 6 Normal Individuals

Name	Coffee				Citral			
	M.I.O.		Duration of Fatigue		M.I.O.		Duration of Fatigue	
	Right	Left	Right (min.)	Left (min.)	Right	Left	Right (min.)	Left (min.)
V. O.	9	9	2	2	8	8	2.5	3
J. B. D.	8	8			7	7	2.5	2.5
C. C. H.	8	8	2	2	7	7	2.5	2.5
H. G. E.	7	7	2.5	2.5	6	6	2.5	3
C. A. E.	9	8	1.5	2	8	8	2	2.5
F. H.	8	8	2	2	7	7	2	2.5

A few examples of the olfactory records of patients and the interpretation of the results of the tests are given in what follows:

Case 1. V. F. Aneurysm of right internal carotid artery.

Clinical Symptoms: Loss of vision in right eye with primary optic atrophy of that side.

Roentgen-Ray Examination: Probable aneurysm of right carotid artery.

Olfactory Tests

Coffee			Citral	
M.I.O. Right 17 Stream Injection for 30 sec. Return of M.I.O.	M.I.O. Left 7 Stream Injection for 30 sec. Return of M.I.O.		M.I.O. Right 16 Stream Injection for 30 sec. Return of M.I.O.	M.I.O. Left 7 Stream Injection for 30 sec. Return of M.I.O.
17 - + * (*)	7 - + *	30''	16 - 0	7 - + *
17 - +	7 - +	1'	16 - + *	7 - +
17 - +	7 - +	1'30''	16 - +	7 - +
17 - +		2'	16 - +	6 - 0

(*) In all of the cases * indicates the duration of fatigue.

Result of Olfactory Tests:

M.I.O. elevated on right, normal on left.

Duration of fatigue not prolonged on right and left.

Conclusion: An extracerebral lesion on the right side compressing the right olfactory nerve.

Case 2. B. B. Pituitary adenoma.

Clinical Symptoms: Primary optic atrophy with loss of vision in right eye, temporal hemianopsia on left.

Roentgen-Ray Examination: Extensive enlargement and destruction of sella turcica.

Olfactory Tests

Coffee			Citral	
M.I.O. Right 30 = 0 Stream Injection for 30 sec. Return of M.I.O.	M.I.O. Left 18 Stream Injection for 30 sec. Return of M.I.O.		M.I.O. Right 18 Stream Injection for 30 sec. Return of M.I.O.	M.I.O. Left 13 Stream Injection for 30 sec. Return of M.I.O.
	18 - 0	30''	18 - 0	13 - +
	18 - 0	1'	18 - + *	13 - ±
	18 - 0	1'30''	18 - ±	13 - ±
	18 - + *	2'	18 - +	13 - + *
	18 - +	2'30''	18 - +	13 - +
	18 - +	3'	18 - +	13 - +

Result of Olfactory Tests:

M.I.O. elevated on right and left but higher on right.

Duration of fatigue not prolonged.

Conclusions: An extracerebral lesion that is involving both extracerebral olfactory pathways, the right more than the left.

Case 3. I. S. Mesial sphenoid ridge meningioma.

Clinical Symptoms: Primary optic atrophy with loss of vision of right eye.

Roentgen-ray of skull negative.

Olfactory Tests

Coffee			Citral	
M.I.O. Right 30 Stream Injection for 30 sec. Return of M.I.O.	M.I.O. Left 6 Stream Injection for 30 sec. Return of M.I.O.		M.I.O. Right 35 Stream Injection for 30 sec. Return of M.I.O.	M.I.O. Left 4 Stream Injection for 30 sec. Return of M.I.O.
30 - 0	6 - + *	30''	35 - + *	4 - 0
30 - + *	6 - +	1'	35 - +	4 - 0
30 - +	6 - +	1'30''	35 - +	4 - 0
30 - +		2'		4 - + *
		2'30''		4 - +
		3'		4 - +

Result of Olfactory Tests:

M.I.O. elevated on right; M.I.O. on left low.

Duration of fatigue not prolonged.

Conclusion: Direct pressure on right extracerebral olfactory pathways by a small lesion which must have existed for a considerable time because there is compensatory hyperacuity of smell on the left side.

Case 4. G. M. Deep left frontal astrocytoma.

Clinical Symptoms: History of transient left hemiplegia six years before; occasional generalized convulsive seizures. Reflexes: Right equal left. Early papilledema.

Roentgen-ray showed calcified tumor in left frontal lobe.

Olfactory Tests

Coffee			Citral	
M.I.O. Right 7 Stream Injection for 30 sec. Return of M.I.O.	M.I.O. Left 11 Stream Injection for 30 sec. Return of M.I.O.		M.I.O. Right 4 Stream Injection for 30 sec. Return of M.I.O.	M.I.O. Left 8 Stream Injection for 30 sec. Return of M.I.O.
7 - 0	11 - 0	30''	4 - + Faint	8 - 0
7 - + Faint *	11 - 0	1'	4 - 0	8 - + Faint
7 - +	11 - 0	1'30''	4 - + Faint	8 - 0
7 - +	11 - + Faint	2'	4 - 0	8 - ?
7 - +	11 - 0	2'30''	4 - 0	8 - 0
	11 - 0	3'	4 - + Faint	8 - + Faint
	11 - 0	3'30''	4 - 0	8 - 0
	11 - 0	4'	4 - + *	8 - 0
	11 - 0	4'30''	4 - +	8 - 0
	11 - 0	5'	4 - +	8 - + Faint
	11 - 0	5'30''		8 - 0
	11 - + *	6'		8 - 0
	11 - +	6'30''		8 - 0
	11 - +	7'		8 - + *
		7'30''		8 - +
		8'		8 - +
		8'30''		7 - 0

Result of Olfactory Tests:

M.I.O. elevated on left. Fatigue prolonged on left.

Conclusion: Left frontal tumor near under surface of frontal lobe.

Case 5. C. H. Right parietal lobe glioma.

Clinical Symptoms: Marked motor and sensory disturbances on left side of body; papilledema.

Roentgen-ray shows calcified tumor in right parietal lobe.

Olfactory Tests

Coffee			Citral	
M.I.O. Right 5 Stream Injection for 30 sec. Return of M.I.O.	M.I.O. Left 5 Stream Injection for 30 sec. Return of M.I.O.		M.I.O. Right 4 Stream Injection for 30 sec. Return of M.I.O.	M.I.O. Left 4 Stream Injection for 30 sec. Return of M.I.O.
5 - 0	5 - 0	30"	4 - 0	4 - 0
5 - 0	5 - 0	1'	4 - + ?	4 - 0
5 - 0	5 - 0	1' 30"	4 - 0	4 - 0
5 - 0	5 - 0	2'	4 - 0	4 - 0
5 - 0	5 - + *	2' 30"	4 - 0	4 - 0
5 - 0	5 - +	3'	4 - +	4 - + *
5 - 0	5 - +	3' 30"	4 - 0	4 - ±
5 - +		4'	4 - 0	4 - +
5 - 0		4' 30"	4 - +	4 - +
5 - 0		5'	4 - 0	
5 - + *		5' 30"	4 - 0	
5 - +		6'	4 - + *	
5 - +		6' 30"	4 - +	
		7'	4 - +	

Result of Olfactory Tests:

Low M.I.O. indicates increased intracranial pressure.

Duration of fatigue normal on left, prolonged on right.

Conclusion: Right hemisphere tumor—not deep.

These records illustrate some of the results of olfactory tests made in patients with verified tumors of the brain. The analysis of the results in the 52 cases which form the basis for this paper has permitted us to draw the following conclusions:

1. *In subfrontal extracerebral growths, the M.I.O. on one or both sides is elevated, while the duration of olfactory fatigue is not prolonged.* If the neoplasm is small and is entirely unilateral, the elevation of M.I.O. is found only on the same side; if the growth is large, the M.I.O. may be raised on both sides and the greater elevation of M.I.O. is found on the side on which the growth or the larger part of the growth is situated. Thus in small aneurysms of the internal carotid artery and mesial sphenoid ridge meningiomas, the M.I.O. is elevated on the affected side and normal on the other side. In the case of a larger aneurysm or tumor, the M.I.O. is elevated bilaterally. Meningiomas attached to the dura of the cribriform plate of the ethmoid or of the tuberculum sellae produce a bilateral elevation of M.I.O. In pituitary tumors that have not extended through the diaphragm of the sella, the M.I.O. is normal, but as soon as the growth has become suprasellar, pressure is exerted upon the extracerebral olfactory pathways and the M.I.O. is elevated unilaterally or bilaterally.

Case 6. Deep left hemisphere glioma.

Clinical Symptoms: For 8 months vague disturbances of left upper extremity. Examination shows hyperactive tendon reflexes on left; papilledema of 4 diopters, bitemporal hemianopsia.

Ventriculography: Lateral and third ventricles displaced to right.

Olfactory Tests

Coffee			Citral	
M.I.O. Right 4 Stream Injection for 30 sec. Return of M.I.O.	M.I.O. Left 6 Stream Injection for 30 sec. Return of M.I.O.		M.I.O. Right 5 Stream Injection for 30 sec. Return of M.I.O.	M.I.O. Left 5 Stream Injection for 30 sec. Return of M.I.O.
4 - + *	6 - +	30"	5 - 0	5 - 0
4 - +	6 - 0	1'	5 - + *	5 - 0
4 - +	6 - 0	1' 30"	5 - +	5 - +
	6 - 0	2'	5 - +	5 - 0
	6 - +	2' 30"		5 - +
	6 - +	3'		5 - 0
	6 - 0	3' 30"		5 - 0
	6 - + *	4'		5 - +
	6 - +	4' 30"		5 - ?
	6 - +	5'		5 - +
	6 - +	5' 30"		5 - 0
		6'		5 - +
		6' 30"		5 - 0
		7'		5 - + *
		7' 30"		5 - +
		8'		5 - +

Result of Olfactory Tests:

M.I.O. low for coffee and for citral.

Duration of fatigue prolonged on left.

Conclusion: Increased intracranial pressure.

A deep intracerebral tumor in the left cerebral hemisphere.

2. In supratentorial tumors within the substance of one cerebral hemisphere the M.I.O. may be normal or smaller than normal, but the duration of homolateral fatigue is definitely prolonged. Apparently the degree to which the duration of olfactory fatigue is prolonged depends upon the extent to which the neoplasm involves deeper parts of the brain. The more deeply a tumor is situated, the longer is the duration of the fatigue produced by the procedure. If the fatigue lasts more than ten minutes, the growth extends to near the midline or actually lies in the midline.

3. In tumors in the substance of one frontal lobe, the M.I.O. is elevated and olfactory fatigue is prolonged on that side. The elevation of M.I.O. is due to pressure upon the extracerebral olfactory pathways of the same side as the growth. Therefore the combination of elevation of M.I.O. and prolonged duration of fatigue must mean that the neoplasm is in the corresponding frontal lobe.

4. In patients with increased intracranial pressure due to tumors of the brain, there is frequently an increased irritability of the olfactory pathways,

Case 7. Glioblastoma multiforme in left frontal lobe extending across midline into right frontal lobe.

Clinical Symptoms: Four weeks' history of right hemiparesis and papilledema.

Olfactory Tests

Coffee			Citral	
M.I.O. Right 11 Stream Injection for 30 sec. Return of M.I.O.	M.I.O. Left 26 Stream Injection for 30 sec. Return of M.I.O.		M.I.O. Right 10 Stream Injection for 30 sec. Return of M.I.O.	M.I.O. Left 25 Stream Injection for 30 sec. Return of M.I.O.
11 - +	26 - 0	30"	10 - 0	25 - 0
11 - 0	26 - 0	1'	10 - 0	25 - 0
11 - 0	26 - 0	1' 30"	10 - 0 ?	25 - 0
11 - 0	26 - 0	2'	10 - + *	25 - 0
11 - 0	26 - 0	2' 30"	10 - +	25 - 0
11 - 0	26 - 0	3'	10 - +	25 - 0
11 - 0	26 - 0	3' 30"		25 - 0
11 - +	26 - 0	4'		25 - ±
11 - 0	26 - 0	4' 30"		25 - 0
11 - 0	26 - 0	5'		25 - +
11 - 0	26 - 0	5' 30"		25 - 0
11 - +	26 - 0	6'		25 - 0
11 - 0	26 - 0	6' 30"		25 - 0
11 - 0	26 - 0	7'		25 - +
11 - 0	26 - 0	7' 30"		25 - 0
11 - 0	26 - 0	8'		25 - 0
11 - 0	26 - ±	8' 30"		25 - 0
11 - + *	26 - 0	9'		25 - + *
11 - +	26 - 0	9' 30"		25 - ±
11 - +	26 - 0	10'		25 - +

Result of Olfactory Tests:

M.I.O. elevated on both sides, left more than right.

Fatigue prolonged on both sides for coffee and on left for citral.

Conclusions: A deeply situated tumor in the left frontal lobe near the midline. The growth has probably extended also into the right frontal lobe.

which is shown by values of M.I.O. smaller than the normal. While low M.I.O. is often seen in patients with increased intracranial pressure, it does not follow that low M.I.O. always means increased tension within the cranial chamber. Low M.I.O.s were frequently observed in diseases of the brain in which there was no increase of intracranial pressure. On the other hand, in patients with papilledema and other evidences of increased pressure, the M.I.O. may be within normal limits.

The study of the sense of smell by the blast injection and the stream injection of odors is therefore of value for the localization of supratentorial tumors of the brain. In some instances the olfactory tests did not show any evidence of a localized lesion and in these instances it was possible to conclude that the patient did not have a supratentorial neoplasm. A more extended experience may show that the tests are of value for diagnosis as well as for localization, but up to the present time, the tests should be used

only for the localization of tumors of the brain. When employed for this purpose, the new olfactory tests may give information which may not be obtained by clinical examination. In unlocalized tumors of the brain, it is possible from olfactory tests to determine that a growth is in or under one or other frontal lobe, and if the growth is not frontal, whether it is in the right or left cerebral hemisphere. In the near future a procedure will be described by which tumors in or under one or other temporal lobe can be localized by olfactory tests.

ERRORS IN THE CLINICAL APPLICATION OF ELECTROCARDIOGRAPHY *

By WILLIAM B. BREED, M.D., F.A.C.P., and JAMES M. FAULKNER, M.D.,
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THE last twenty years have seen an enormous growth in the use of the electrocardiograph as a diagnostic instrument. From a cumbersome and expensive machine available only to the larger hospitals and clinics have been developed models which are light enough and cheap enough to be entirely practicable for use in office or home. It is estimated that there are three thousand electrocardiographs in active use in this country today and the number of instruments is rapidly increasing. A result of this tremendous growth has been that we as internists are being called upon more and more to assess the clinical significance of electrocardiographic abnormalities.

When one examines the body of data on which much of our diagnostic and prognostic criteria in electrocardiography rest, one is struck by the paucity of suitable control material. Quite naturally most of the studies which have been made in this field were carried out on patients who came to a clinic because of suspected heart disease. The dire prognosis which soon came to be associated with many electrocardiographic signs was therefore based in part on statistics from a selected group heavily weighted with bad risks. The very fact that an electrocardiogram was taken usually meant that the patient had either symptoms or signs suggestive of heart disease.

One example of overemphasis of the seriousness of an electrocardiographic finding has been in the case of bundle branch block. In the beginning we were inclined to assign a bad prognosis to every case exhibiting this sign, but as the years have gone by we have seen more and more patients with bundle branch block outliving their brief expectancy of life by many years. Although such signs of course merit serious consideration, our experience has made us more cautious about attaching prognostic significance to isolated electrocardiographic abnormalities.

From the point of view of negative evidence it has been recognized from its earliest application to clinical diagnosis that the electrocardiogram may be normal in the presence of obvious organic heart disease and consequently the importance of negative records has been duly discounted.

The subject of this paper deals with the occurrence of certain positive abnormalities—perhaps better termed peculiarities—of the electrocardiogram in the absence of organic heart disease. The importance of these peculiarities lies in the fact that they may simulate changes associated with serious cardiac disorders and thus may lead to grave diagnostic error. We

* Presented at the Detroit meeting of the American College of Physicians, March 3, 1936.

do not include in this discussion the alterations in the electrocardiogram dependent on infections, toxemia or anoxemia.

Abnormalities in the contour of the electrocardiogram result from abnormal relationships between the pathways of conduction and the recording electrodes. Therefore, in addition to intrinsic lesions of the conducting system and myocardium, unusual positions of the heart in the chest may be reflected in peculiar electrocardiographic patterns.

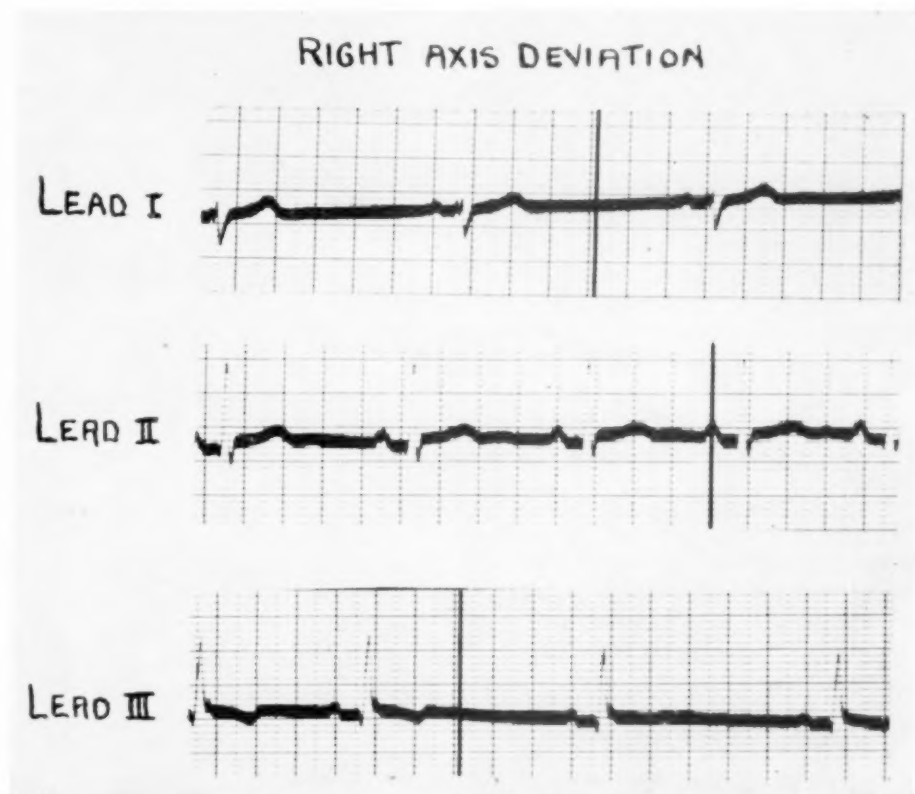


FIG. 1. Right axis deviation in a normal vertical heart.

The effect of position of the heart on the electrical axis has been too well recognized to require more than passing comment. Figure 1 is a record of an individual with a normal heart in a vertical position. It shows right axis deviation.

Figure 2 shows left axis deviation resulting from a transverse position of the heart in a normal, healthy young man of sthenic habitus. Deep inspiration swings the electrical axis into the normal zone. Less well recognized is the fact that high diaphragm may cause the development of a deep Q-wave and an inverted T-wave in Lead III.

In rare cases the position of the heart may determine the direction of the

T-wave in Lead II. The following case, presented through the courtesy of Dr. Howard B. Sprague, illustrates this condition.

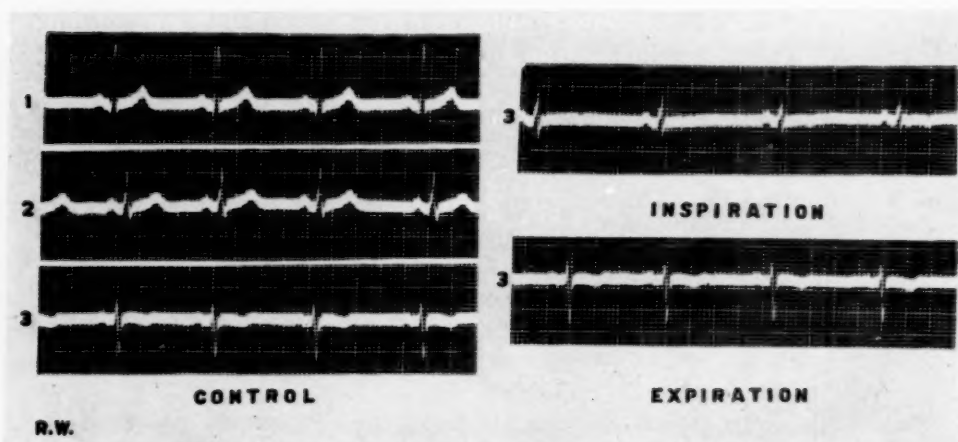


FIG. 2. Left axis deviation in a normal transverse heart. Note shift in axis to normal with depression of the diaphragm in inspiration.

G. C., a 19 year old boy, was referred to him in December 1935 because on routine examination as a college freshman he was found to have tachycardia and hypertension. His past history was irrelevant. He played football in high school. He had no symptoms of any sort.

Physical examination in general was negative. The heart was not enlarged. The action was rapid with marked sinus arrhythmia. No murmurs were heard. Blood pressure was 135 mm. Hg systolic, 90 mm. Hg diastolic. Roentgen-ray examination showed the heart to be normal in size, shape and position.

Figure 3 illustrates the marked effect of change in position of the heart on the T-waves particularly in Lead II. On deep expiration the T-waves previously inverted became upright. Because of its peculiar lability and in the absence of any other evidence of heart disease it was concluded that the inversion of the T-wave in Lead II did not signify myocardial disease and the boy was allowed to resume full activity.

Another type of electrocardiographic peculiarity is caused by nervous influences upon intraventricular conduction. The first case of this type was reported by Dr. Frank N. Wilson¹ of Ann Arbor in 1915. A group of them which correspond to a fairly distinctive pattern were described by Wolff, Parkinson and White² in 1930 and have come to be known by the term "functional bundle branch block." This condition is characterized by a very short P-R interval and prolonged intraventricular conduction with slurring of the initial phase of the ventricular complex. The mechanism appears to be dependent upon a certain amount of vagal tone and may be abolished by atropine, adrenalin or exercise. Clinically it is usually associated with a history of paroxysmal tachycardia but with no other cardiac

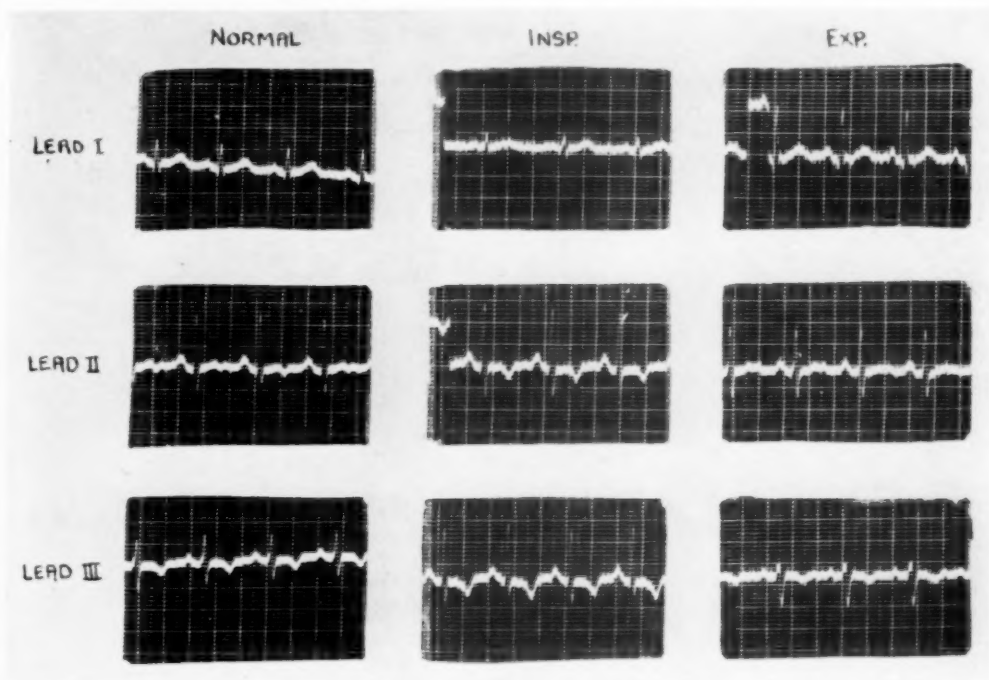


FIG. 3. Peculiar T-wave in Lead II markedly altered by deep breathing. Apparently normal boy.

abnormality. Figure 4 is an illustration of functional bundle branch block in an Italian laborer of thirty-five. He gave the characteristic history of frequent attacks of paroxysmal tachycardia but no other evidence of heart disease. The records were taken a few days apart and show the characteristic features of the condition in the one record and an entirely normal picture in the other. In some subsequent records these changes are seen to appear and disappear within a few seconds.

Figure 5 illustrates a closely similar condition with a short P-R interval and prolonged intraventricular conduction. It is from a patient of Dr. Paul D. White.

When first seen he was an 18 year old boy and a member of a college freshman swimming team. He had a history of paroxysmal tachycardia. Physical examination was negative except for reduplication of the first sound at the apex of the heart. Roentgen-ray revealed no abnormality in the size, shape, or position of the heart and the basal metabolic rate was normal. An electrocardiogram taken in 1936, eight years later, showed the same abnormalities and the same decrease in the amplitude of the T-waves after exercise.

In a third group of cases transient inversion of the T-waves in Leads I and II without other changes has been observed in the absence of organic heart disease. As Graybiel and White³ pointed out, this is often associated with neuro-circulatory asthenia, paroxysmal tachycardia or thyrotoxicosis.

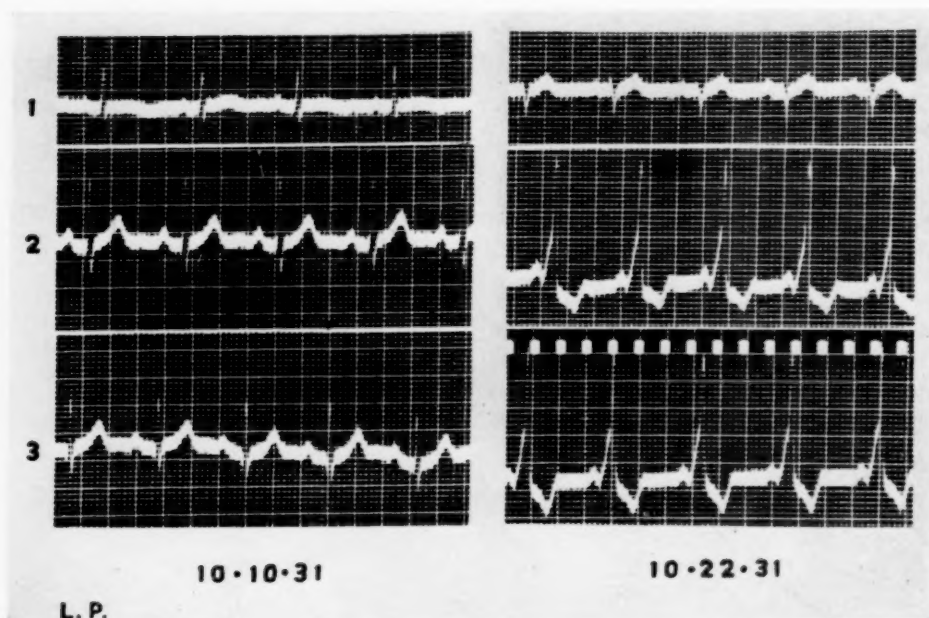


FIG. 4. Normal mechanism and "functional bundle branch block" in the same individual.

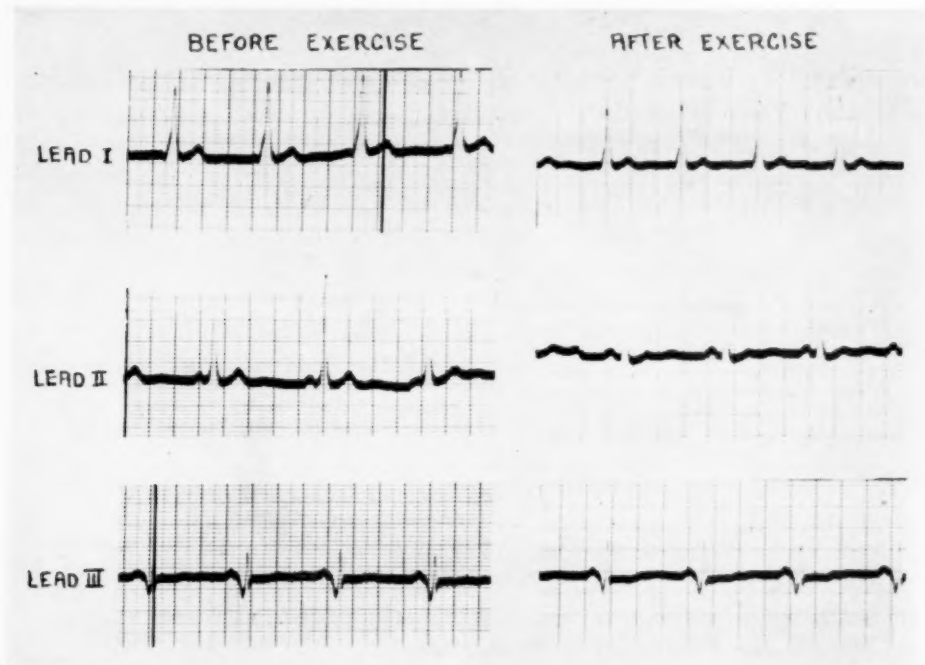


FIG. 5. Intraventricular block with short P-R interval in an apparently healthy youth.

The following case is an illustration of this type of disturbance:

In the fall of 1934, A. P., a 16 year old boy, had presented himself with the story that his local doctor had forbidden him strenuous exercise because of rapid heart action. He himself sometimes felt his heart pound but not particularly when active. He did not know whether the action was rapid or irregular. He had no other complaints. He had had a normal development without rheumatic fever, scarlet fever or chorea.

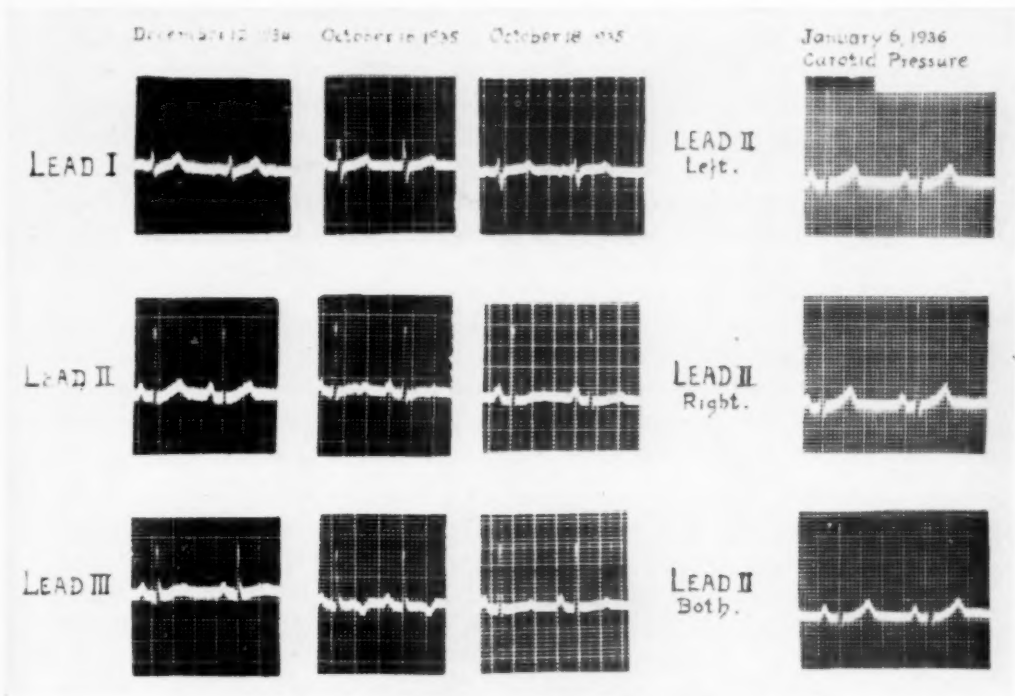


FIG. 6. Transient changes in T-waves particularly in Lead II unassociated with any clinical evidence of disease.

Physical examination at that time showed no evidence of disease. The heart was not enlarged, the rhythm and sounds were normal, with a rate of 72 at rest. There were no murmurs. The blood pressure was 120 systolic and 65 diastolic. The response of the heart rate and the blood pressure to exercise was normal. A seven foot plate of the chest showed the heart normal in size and shape, and the aorta normal in appearance. Electrocardiogram showed normal mechanism, rate 98. The auriculo-ventricular and intra-ventricular conduction times were within normal limits and all T-waves were upright and of normal shape.

A diagnosis of irritable heart was made and he was allowed to resume strenuous activity—to include football playing. He was seen next in February 1935, five months later, at which time no mention was made of his heart, and physical examination was again negative.

In October 1935, one year after his first visit, he appeared because when warming up on the sidelines of a football game he would feel his heart pound and would be momentarily short of breath. In a few seconds these symptoms would pass, he would enter the game and play hard with no symptoms. He had had an unusually active preceding summer and avowed he never felt better.

Physical examination revealed a normal sized heart, rate 78, normal rhythm, no murmurs, blood pressure 120 systolic and 80 diastolic. The electrocardiogram, however, showed a definite change from that made one year previously (figure 6). The record now showed a peculiar diphasic character to the T-wave in Lead II and a considerable late inversion of the T-wave in Lead III.

This was very disconcerting. Because of our conviction that this boy had no myocardial or coronary disease as suggested by the electrocardiogram we sent him running up and down two flights of stairs. On his return to the laboratory there appeared a slight definite change toward normality. This tendency to change under observation, especially following a speeding up of the circulation confirmed us in our opinion that the electrocardiogram was recording only functional changes, and so he was again sent back to the football field. A check-up on January 6, 1936, after a strenuous athletic season, now showed a completely normal tracing. To test the effect of vagal stimulation on the mechanism, pressure was applied to the left, right, and to both carotid sinuses. No changes in the T-waves were produced by these measures, although the rate was definitely slowed.

The conclusions to be drawn from these experiences are that when isolated electrocardiographic abnormalities occur in the absence of any other signs of heart disease they must be viewed with skepticism. The functional nature of some of these may be demonstrated by appropriate measures such as by exercise, administration of atropine or deep breathing.

DISCUSSION

Such observations as the foregoing illustrate anew the dangers of interpreting an electrocardiogram without full knowledge of all the other clinical features of the case. The testimony furnished by the electrocardiogram can be properly evaluated only when all the evidence is in, or occasionally it will deceive us. It will always tell the truth but never the whole truth.

Now that this delicate instrument of precision is becoming an every day office accessory of the internist, it may be hoped that it will lose some of the aura of infallibility which hung about it in its laboratory days. It may then assume its rightful position, not as a court of last appeal in cardiac diagnosis, but as a very valuable adjunct to physical and roentgen-ray examinations.

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PUBLIC HEALTH CONTROL OF SYPHILIS *

By THOMAS PARRAN, JR., M.D., Commissioner of Health, New York State,
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As one after another of the epidemic diseases has declined or disappeared under the impact of public health effort, it is natural that the same technics should be directed against other major causes of sickness and death. Moreover the success of past and current public health measures has engendered the confidence of the tax-paying public which will support extension of community action into fields heretofore reserved to private effort.

These two facts make it inevitable that the public health control of syphilis should be the central problem now faced by health departments. In undertaking any public health measure, those of us responsible for securing and expending public funds must consider the extent of the hazard to health and life, the controllability of the disease, and the cost of effective control efforts.

EXTENT OF THE SYPHILIS PROBLEM

From the mass of conflicting statistics and statements about syphilis, it is difficult to sort out dependable facts. This is due both to the nature of the disease and the different methods of stating its extent. Syphilis often is a subclinical infection with an unrecognized onset. It has periods of latency, and the end-point or cure frequently cannot be determined. Both the past and the present true attack rates are still the subject of conjecture. Although it shortens the life span of its victims, the total effect on mortality is not known.

Moreover, in expressing the amount of syphilis in a community, one may refer to the number of clinically recognized cases which are under treatment at a given time; the attack rate of clinically recognized cases which occur in a specified period; or the findings from serological and clinical surveys among special groups. Since in every community an unknown number of cases are not diagnosed and treated; and since surveys of limited groups are made by serological tests of varying sensitivity; and since such groups are not representative in age, sex, and other respects of the whole population, none of these methods gives a complete picture.

Add to these inaccuracies the geographic, racial, sex, social, and age variation in syphilis prevalence, and the complexity of the problem becomes apparent. In fact, it probably is easier to eradicate syphilis in a population than to determine its exact prevalence and distribution. In spite of these inaccuracies and uncertainties, certain facts are clear and certain conclusions are warranted concerning the extent of the syphilis problem. These facts together indicate that the statement of Sir William Osler, that syphilis ranks

* Read at the Detroit meeting of the American College of Physicians, March 3, 1936.

with tuberculosis and cancer as a major cause of death, is as true today as it was when he made it.

In upstate New York a census of all cases under treatment by all physicians, hospitals, clinics and other institutions was made in 1927 and repeated in 1930 and 1935. In the last two surveys data were secured also as to the number of new cases which were diagnosed for the first time during the month of April.

The total of cases under treatment *increased* from approximately 12,000 in 1927 to approximately 17,000 in 1935 (43 per cent); while cases of early syphilis *decreased* from 3,415 to 2,029 (43 per cent) during the same period.

The total of cases diagnosed for the first time in April 1935 was 1,644 which, when compared with 1,899 diagnosed in a similar period in 1930, constitutes a decrease of 19 per cent. Early syphilis cases diagnosed for the first time in April 1935 were 462, as compared with the 1930 total of 854, a decrease of 46 per cent.

The prevalence and attack rates in upstate New York as shown by our surveys are much lower than in southern states and in cities with large negro populations, but much higher than in certain mid-western rural areas.

Studies by Nelson in Massachusetts show also a decline in new cases of the disease in recent years, but a continued increase in total cases.

The decline in early cases in these two states from which recent reports are available suggests that at last the results of control efforts are apparent. The continued increase in the total of cases newly diagnosed impels caution, however, as to full acceptance as yet of this conclusion. A disturbing fact apparent from the data collected in this and other countries is the large proportion of late syphilis in the total of first diagnoses and clinic admissions. In Great Britain, for example, with accurate histories on admission for all clinic cases, more than one-half of the new admissions are cases of late syphilis. Case finding early in the disease leaves much to be desired.

Although recent reports from Massachusetts and New York suggest a decrease in new cases of syphilis, the data available to the Public Health Service from the country as a whole do not indicate a decline. From Great Britain and the Scandinavian countries, on the contrary, reliable reports are available showing that syphilis in recent years has declined markedly, and in the Scandinavian countries the disease now shows only a small fraction of its former prevalence. With frank skepticism, I undertook a study last summer of their data, their methods, and results. Three critical colleagues confirm my statement that the Scandinavian reports are genuine. Syphilis there has become a rare disease. In Sweden, with a population of 6,100,000 (almost the same as upstate New York), there were just 431 cases of the disease in 1934; in the first half of 1935 there were only 200 cases. Multiply the population and cases by 20 and the data are comparable with those for the United States. If the rate for Sweden were applied to the whole population of the United States, we would have annually only 8,620 cases. Compare this with the Public Health Service estimates of 420,000. The

rate in Sweden now is only one-tenth of the rate 15 years ago. That inadequate reporting is not a factor is confirmed by the continued high prevalence of gonorrhea, amounting to approximately 12,000 new cases in 1934. This fact, too, makes it clear that medical measures rather than moral restraints have brought about the decline in syphilis.

In Denmark an almost comparable decline has been recorded. In that country all Wassermann tests for the whole country are done in the one State Serum Institute, where complete records have been kept of every examination, positive and negative, during the past 16 years. Denmark has a population of 2,600,000. In 1933 syphilis cases totalled 648. At the peak of the post-war epidemic in 1919 there were 7,024 cases. In Copenhagen the decline has been even greater—from 2,189 to 181. Here, too, the prevalence of gonorrhea has continued high.

In Norway, data for the country outside of the capital, Oslo, are incomplete. In this city, however, the cases per 100,000 population decreased from 360 in 1919 to 30 in 1935.

In Great Britain, where there is no reporting of cases but where a large percentage of the total is treated in public clinics, new admissions have declined by more than one-half since 1920. The 20,692 new admissions to clinics in Great Britain and Wales in 1934 represent an admission rate of 54.3 per 100,000 population. This should be compared with the upstate New York clinic admission rate of 112.6 for the same period.

While the methods in these countries differ in many respects, the provision of public clinic facilities of a good quality, available to all patients, is the factor common to each. In addition, the Scandinavian countries require notification of cases, and treatment is compulsory. In Sweden the careful investigation made of sources of infection is a noteworthy feature.

CONTROLLABILITY OF SYPHILIS

It is not surprising that countries which have undertaken systematic control measures have gotten results, since the facts concerning syphilis argue for its controllability. The causative agent is known; a diagnosis can be made as soon as the case is infectious; we have serological tests which will discover otherwise latent cases; in the arsphenamines, we have remedies which will speedily sterilize the infectious case. Unlike such diseases as typhoid fever, syphilis is spread singly from person to person by intimate contact. The source of infection and those exposed usually are known to the patient.

Compare these facts with tuberculosis, a disease which has declined by two-thirds during the past 30 years. For tuberculosis, there is no specific method of cure or of rendering the patient non-infectious. Diagnosis of the early case is costly and difficult. The infectious agent is widely disseminated in the population. In spite of these greater difficulties, the practical control and even eradication of tuberculosis in this country is a goal

clearly in sight. The great difference between these diseases, however, is that, in the case of tuberculosis, we have promoted public knowledge of the disease; mobilized the profession; created public facilities; and organized community programs of control.

In spite of knowledge concerning syphilis, which seems adequate for control, we must not lose sight of certain biologic facts which make the problem difficult: the obscure nature and transitory character of the initial lesion; the tendency of the disease to relapse under inadequate treatment; the possibility of second and completely blind infections; the unknown rôle of the chronic carrier as a factor in spread; and the possible reversion of the organism to a more virulent form. These factors are important and need further study. Since our present methods do not appear to have brought about a decline in syphilis prevalence, it is fair to ask if we have neglected to use to best advantage all available weapons.

EPIDEMIOLOGICAL APPROACH

During recent years, the studies of Munson in New York and of Smith and Brumfield in Virginia demonstrate clearly that, by the use of the epidemiological method, undiscovered sources of infection can be found and brought under treatment. Evidence has accumulated also which shows that syphilis does not spread evenly in the population, but that it is kept alive and spreads chiefly by a series of small epidemics. Munson traced more than 30 such local outbreaks, averaging four or five cases each, most of which were not under treatment. Smith and Brumfield have shown that from 157 new cases of early syphilis 345 contacts or potential sources were named (representing 278 persons), of whom nearly one-half were located and brought under treatment. Of these cases, all were in the early infectious stage of the disease and had not been under treatment previously. These methods have been tried in New York State in recent years with results sufficiently gratifying to warrant the state-wide application of the principle. In the epidemiological method, we have an unused instrument for the control of syphilis which, in my opinion, is of as much value as the Wassermann test or the arsphenamines.

NEW YORK PROGRAM

Before starting our program, it was discussed with the Public Health Committee of the State Medical Society, and many details worked out with the advice of its members. As finally agreed upon, it was approved by this committee and the Executive Committee of the State Society.

Our syphilis control program has four major objectives: (1) The notification of cases; (2) intensive and complete investigation and supervision of sources of infection, cases and contacts; (3) the provision of facilities for adequate diagnosis and treatment; (4) professional and public education.

In New York City essentially the same plans are being developed but modified to fit the particular needs of that large metropolis.

For administrative purposes, the State (outside of New York City) is divided into 33 districts comprising the 12 cities of more than 50,000 population, the five county departments of health and 16 state health districts. The program is carried out by the city and county departments of health with state-aid if State standards are met. Outside of the large cities and the five counties with departments of health, state-aid is given to local clinics, but reports are made directly to the state district office, and state personnel is used for the epidemiological work.

CASE REPORTING

The starting point is a state-wide system of approved laboratories. Whenever a physician diagnoses or suspects the existence of syphilis or of another communicable disease, an appropriate specimen must be sent to an approved laboratory accompanied by information as to whether the specimen is for diagnosis or treatment control, the stage of the disease, and other pertinent facts. The laboratories are required to submit copies of all positive reports to the local health officer or the state district officer. Physicians are required to make a case report of each case of syphilis, giving sex, date of birth, and address, but it is not necessary for the name to be given. Thus the identity of the coöperative private patient is safeguarded. These reports are checked against the positive laboratory findings to insure completeness.

Physicians are required, however, to report by name any lapsed infectious case, and health department nurses are available to follow up such lapsed cases and return them to their physician for further treatment. Another service is the furnishing of free arsphenamines and bismuth to private physicians for private patients, as well as to clinics.

When a case of smallpox seeks treatment, the first impulse of any good physician is to call the health officer. Is it too much to hope that we can create the same interest in the source of early syphilis? Is it unreasonable to ask that an obligation to the community no less than to the patient be assumed in this as in other infectious diseases?

All cases of syphilis are classified into three categories: (a) early syphilis (less than one year since onset); (b) other potentially infectious cases; (c) late non-infectious cases. The term "potentially infectious" is applied to the following types of cases regardless of the presence or absence of visible lesions:

1. All patients with acquired syphilis who have received less than 20 injections each of an arsphenamine and a heavy metal, or equivalent treatment, until five years have elapsed since onset.
2. All female patients with acquired syphilis inadequately treated, until the menopause has been reached.

3. All patients with early congenital syphilis.

Efforts to determine sources of infection are limited to early syphilis. Investigation of contacts, however, and supervision of cases are extended to include also all potentially infectious cases, but with major emphasis on persons 15 to 30 years of age and cases of less than 2 years' duration.

EPIDEMIOLOGICAL WORK

In each of our 33 districts a trained medical officer with one or more nurses and sufficient clerical assistance is responsible for the syphilis epidemiological work. When a physician reports a case in private practice, the medical officer goes or telephones to the physician himself and asks him either to permit the health department to investigate the case or to make this investigation himself in order to locate, if possible, the source of infection. If the physician elects to assume the responsibility, he again is given the choice of getting the source of infection and contacts under treatment, or permitting the health department to do it. After six months' trial in our larger cities, I am happy to report that in practically no instance have the physicians failed to cooperate. It is beginning to be apparent, however, that the record of the private physician in ascertaining sources of infection is not as good as that of the trained epidemiologist. An epidemiological record card is executed for each early case, which is comparable in completeness to the records used in the investigation of typhoid fever, for example.

No investigation of an early case is acceptable unless the source of infection is found, or unless satisfactory evidence is submitted to establish beyond reasonable doubt that this individual cannot be identified and located. Results to date indicate that, in from 20 to 30 per cent of all cases of early syphilis, the source of infection can be located and brought under treatment.

APPROVED CLINICS

An essential part of our program is to elevate the quality of clinic service. Those clinics which meet prescribed standards are designated as "approved clinics." * Until recently most physicians have served in syphilis clinics without compensation. Provision now is made for paying all such physicians. The rate of payment varies, but averages about \$10 per session.

The following classes of patients are eligible for treatment at clinics irrespective of whether or not they are residents: (a) any patient for initial diagnosis and emergency treatment if found to be infectious; (b) any patient

* Standards for "approved clinics" may be summarized as follows: They must be conveniently located with adequate quarters and separate waiting rooms or separate sessions for men and women. Records containing prescribed minimum information must be kept. The treatment of early syphilis must be a continuous system and in conformity with modern accepted practice. Spinal fluid examinations must be performed whenever possible before the patient is ready for discharge. In the larger centers facilities for cardiovascular and other examinations must be provided. Each clinic must have adequate medical, nursing and clerical personnel. In each city daily clinic service must be provided with at least one evening session per week, and facilities must be provided to determine the financial status of patients.

unable to pay a private physician for treatment; (c) any patient referred by physician for consultation, such case to be returned to the referring physician with examination reports and advice for further treatment. The acceptance of non-resident patients and the introduction of consultation for the general practitioner as a function of the clinic are new features.

Definite requirements are made concerning the reporting of cases which lapse for more than one week, and an automatic procedure of follow-up is established. Wherever possible, improvement of existing clinics attached to hospitals is sought, rather than the setting up of separate clinics.

There are approximately 120 syphilis clinics in upstate New York, and we are now engaged in studying these clinics and specifying the changes necessary to qualify for approval and state aid.

In the centers of population too small to support a clinic service, the local health officer is required by law to provide treatment of any person with a venereal disease unable to pay a private physician. For this service he is entitled to payment at rates comparable to those paid for other public medical services.

EDUCATION

Major emphasis thus far has been put upon professional education. This includes the training of physicians and nurses in the public health and clinical aspects of the problem.

An extension course in social hygiene was given to more than 1,000 public health nurses two years ago. This was followed last year by a summer course at Syracuse University for 70 nurses selected for this special work in clinics and health departments. Another such course will be held this summer for a larger group. In addition, we are assembling a corps of young physicians and giving them special training in public health and in the epidemiological method of syphilis control. A number of the leading syphilologists in the State are assisting us on a part-time basis as consultants in promoting the organization and quality of clinic service, and in professional education.

A series of regional institutes will be held this year primarily for clinic physicians. Attendance is promoted by compensating these physicians for time lost from practice. These institutes will be open to other interested medical men. Moreover, a number of County Medical Societies are holding for practitioners postgraduate courses in syphilis therapy. By these several methods we hope to compete with the pharmaceutical "detail men" in teaching the general practitioner how to treat syphilis.

For several years we have had the active coöperation of the State Committee on Tuberculosis and Public Health in promoting public interest and knowledge of syphilis. Some progress has been made in breaking down the barrier of public ignorance and apathy. Our Governor and Legislature have been willing to provide funds. They have been convinced that the cost of a syphilis control program is less than the cost of continued neglect. The

newspapers, and recently the National Broadcasting Company have permitted the word syphilis to be used. Health departments and physicians must seize the opportunity and be prepared to furnish needed information. Yes, the word *syphilis* must be spoken, heard, printed, understood.

SUMMARY

The prevalence of syphilis in the United States continues to be high, and its control is the most urgent public health task with which health authorities are confronted.

The Scandinavian countries, and Sweden in particular, by organized national effort have accomplished a modern miracle in medicine: the practical eradication of syphilis.

The epidemiological method of locating infectious sources is an unused weapon, but potentially as valuable as the arsphenamines and serodiagnosis.

New York State is undertaking a serious state-wide control program with full coöperation of the medical profession.

What the health department is doing in New York can and should be done in every State. Available Federal funds for Social Security make it possible.

In the public health control of syphilis, the members of the American College of Physicians have an opportunity this year, each in his own community, to sponsor and support a great work for a high purpose, with assurance of good results to the public.

THE CLINICAL ASPECTS OF AMYLOIDOSIS *

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INTRODUCTION

FROM the nosological aspect generalized amyloidosis has not received its due recognition. It has hitherto been largely viewed as an ominous sequel of chronic suppuration, with cachexia, anemia, swelling of the liver and spleen, and albuminuria as the most prominent clinical expressions. In recent years, new data have been established which have widened the diagnostic basis of this disease. These are the recognition: (1) of primary amyloidosis; (2) of so-called atypical amyloidosis; (3) of the relation of general amyloidosis to "nephrotic," or better termed, hypoproteinemic states; and (4) the establishment of the Bennhold Congo red test. These viewpoints and the opportunity to observe a considerable number of cases of amyloidosis, both primary and of unusual etiology, have stimulated this study.

A. MORBID ANATOMY

The amyloid substance is deposited in the mesenchyme and more particularly in the reticular and collagenous tissues of the periglandular and pericapillary structures. The reticulo-endothelial system is usually profoundly affected. Epithelial tissues are comparatively free from amyloid invasion. Friedreich and Kekulé¹ first showed that the amyloid substance was protein in nature. For a long time, amyloid was supposed to be a compound of protein with chondroitin-sulphuric acid, but Hanssen² who studied amyloid in pure form found no chondroitin-sulphuric acid. Eppinger³ in his chemical analysis of a solitary amyloid mass, found within a liver, determined that the dried material contained purines, diamine acids and much tyrosine. There was no carbohydrate, phosphorus or sulphur. Apparently amyloid is not always uniform in chemical composition, because in some of the atypical forms of amyloidosis the staining reactions are bizarre (Lubarsch⁴).

The organs most frequently involved in generalized amyloidosis are, in the order of frequency, the spleen, liver, kidney, suprarenals, and lymph nodes. This incidence corresponds to that found in experimental amyloidosis (Jaffé⁵) and to that found in horses used in antitoxin production (Doerken⁶). Less frequently amyloid is deposited in the intestines and pancreas. Lubarsch never saw amyloid in the brain. In the atypical form of amyloidosis amyloid has been found in almost every organ of the body: the tongue (Pick⁷), the bone marrow (Gerber⁸), the skin (Königstein⁹),

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From the Service of Dr. B. S. Oppenheimer, Mt. Sinai Hospital, New York City.

the muscles (Warren¹⁰), the heart (Budd¹¹), and in tumors (Weber,¹² Glaus,¹³ Hueter¹⁴).

The detection of amyloid in tissues is entirely colorimetric, and depends upon the histological reaction of this substance to the methyl violet stain and to iodine.

Etiology. That amyloidosis follows chronic suppuration is well known. Of 112 autopsies in Montefiore Hospital in which amyloid was present, Rosenblatt¹⁵ found that in 100 there was an associated tuberculosis. This represented 25 per cent of all patients dying with this disease. Of the remaining 12, three had no apparent cause, two were associated with carcinoma of the lung and secondary suppuration, one was associated with a chronic osteomyelitis, three with pyelonephritis, one with carcinoma of the stomach, one with leukemia and one with tabes dorsalis. Of 100 cases of amyloid disease involving the kidney, reported from the Philadelphia General Hospital by Dixon,¹⁶ 78 per cent were associated with tuberculosis of the lungs or bones, 9 per cent with malignant tumors, 5 per cent with empyema, 2 per cent with chronic arthritis, 2 per cent with osteomyelitis, 1 per cent with bronchiectasis, 1 per cent with lung abscess, and in 3 per cent the cause was unknown.

At Mt. Sinai Hospital, amyloid change was found in 42 autopsies from the year 1916 to the present. Of these, 11 were caused by tuberculosis of the lungs, 10 by lung abscess or chronic bronchiectasis, three by chronic osteomyelitis, four by neoplasms, two by Hodgkin's disease and one each by subacute bacterial endocarditis, lues of the aorta and liver, chronic ulcerative colitis, tuberculous osteomyelitis, tuberculous pyonephrosis, tuberculous entero-colitis, perinephritic abscess, general tuberculosis, tuberculous coxitis. Two cases were primary. Of the total, 16 were caused by tuberculosis. This report does not include clinical cases of amyloidosis observed at Mt. Sinai Hospital during this time, but it represents a valid cross section of the incidence in relation to etiology.

There is an interesting association between amyloid and myeloma. Magnus-Levy¹⁷ in 1931 collected 19 such cases. The amyloidosis may be generalized but more often it is localized in unusual sites, such as the muscles, the dura mater, the abdominal wall, the intestines, the bones, tongue, esophagus, etc. Magnus-Levy regards the amyloid substance and Bence-Jones protein as chemically related. He found small quantities of Bence-Jones protein in myeloma tissue especially in crystalline form. He does not believe that the Bence-Jones protein is transported. He also found Bence-Jones protein in the body fluids, in the blood serum, in serous effusions and in the bone marrow, and only rarely in the liver, spleen and kidneys. The reason it is found only in small quantities in these fluids is, he believes, because it is rapidly formed and excreted. Bell¹⁸ reports a case of amyloid with myeloma in which the extensive amyloid infiltration of the muscular wall of the intestine caused obstruction.

The association of generalized amyloidosis with malignant blastomata is not uncommon. Usually the tumor shows extensive necrosis. Lubarsch saw amyloid 20 times in a series of 398 cancers, and in a large percentage of experimental mouse cancers. We are not referring here to the cases of localized microscopic or extensive amyloid infiltration of blastomata, usually myeloma, that have been reported (Weber, Glaus, Hueter).

The occasional association of amyloidosis with non-suppurative maladies is not always to be regarded as cause and effect. For instance, the simultaneous occurrence of chronic deforming arthritis and amyloidosis is reported too infrequently (Dixon, Rosenblatt, Perla and Gross¹⁹) (cases 1 and 2 in my series may be included) to be more than an accidental association. In all likelihood, the arthritis is not the cause of the amyloidosis, rather both conditions are simultaneous reactions to the same insult.

Primary amyloidosis forms a not inconsiderable section of all reported cases, especially of the localized or atypical variety, and offers a difficult problem for diagnosis. Such primary cases comprise a distinct nosological entity which requires serious consideration.

CASE REPORTS

Case 1. S. H., aged 57, was admitted to the service of Dr. B. S. Oppenheimer, September 14, 1934. The previous history was irrelevant. Four years ago, following the onset of menopause, the patient developed pain, swelling and stiffness of the joints; many of the joints showed an effusion. Subsequently the joints of the hands and feet became deformed. During the past three years there has been swelling of the lower extremities and increasing loss of weight. Five weeks previous to hospitalization she developed anorexia, nausea and vomiting and she also noted that her skin was becoming dark. On examination, in addition to the pigmentation of the skin, there was a bilateral conduction auditory defect, yellowish exudates in the right fundus, a heart enlarged to the left with sounds of poor quality; a systolic murmur was heard over the precordium but loudest at the base; the blood pressure was 110 systolic and 60 diastolic. The peripheral vessels were not sclerosed. The liver was enlarged, reaching 3 cm. below the costal margin. The muscles of both hands were atrophic; there was ulnar deviation, spindle shaped fingers and swelling of the metacarpal joints. The knee joints were red, swollen and tender. There was tenderness of both shoulder joints, and slight edema of both lower extremities. The hemoglobin was 60 per cent, red blood cells 3,400,000, white blood cells 8,000, polymorphonuclears 50 per cent. The urine showed a specific gravity of 1.014 after the concentration test, there was a heavy precipitate of albumin on boiling and casts were present. The blood cholesterol was 290 mg. The urea 27 mg. The total blood protein was 6.2 per cent, of which the albumin fraction was 2.3 per cent and the globulin 3.9 per cent. The Congo red test showed 70 per cent tissue retention. A diagnosis of primary amyloidosis was made. Liver extract was given intramuscularly and by mouth. For a while there was some general improvement. An examination one year later revealed no appreciable change from her previous condition.

Summary. A woman of 57 with a history of deforming general arthritis of four years' duration, the onset of which was followed shortly by symptoms of the so-called nephrotic syndrome with anemia and weakness and simultaneous enlargement of the liver and spleen. The Bennhold Congo red test confirmed the clinical impression that the case was one of generalized amyloidosis. No cause was discoverable. One year later the condition of the patient was unchanged.

Apparently the association of amyloidosis with chronic arthritis is not as rare as generally regarded. The following instance shows that it may occur even in early childhood.

Case 2. A child, aged $2\frac{1}{2}$ years, was admitted to the service of Dr. B. Schick on April 18, 1933 and discharged January 2, 1935. She had suffered with convulsions since the age of one. Shortly after the last convulsion pain in the left thigh and knee appeared followed by pain in the left elbow. Fever appeared two weeks before admission.

On admission she had a temperature of 101.6° F. There were stiffness and tenderness of the lower cervical spine. The left wrist was swollen, hot and tender. The left ankle was swollen and tender. The liver and spleen were not palpable. A soft systolic murmur was heard in the fourth interspace, not transmitted. The urine was normal. The hemoglobin was 61 per cent, red blood cells 3,900,000, white blood count 18,800 with a normal differential count. The sedimentation rate was 31 minutes. The electrocardiogram showed sinus tachycardia. Roentgen-rays of the joints showed no pathologic changes.

For the next nine months the child ran a febrile course, then she became afebrile. The fever reached 104° and she had occasional chills. Blood cultures on several occasions proved sterile. There was progressive loss of weight. Roentgen-rays of her knees taken four months after admission showed marked swelling of the soft tissues with some periosteal thickening of the upper end of the right ulna. A roentgenogram of the chest showed nothing abnormal. The use of typhoid vaccine and removal of the tonsils had no effect upon the progress of the disease. About nine months after admission the liver became palpable two fingers' breadth below the costal border. The urine contained large amounts of albumin. A Congo red test showed 50 per cent retention at the end of one hour. There was 65 per cent excretion of phenolsulphonephthalein at the end of two hours. The concentration of urine was normal. The sedimentation time varied between 5 and 15 minutes. A Congo red test done eight months after admission showed 100 per cent retention. Roentgen-rays about this time showed marked atrophy of all the bones in both knees. The epiphyses were large and irregular, and there was considerable calcified material between the epiphyses. Wassermann tests were negative.

Case 3. C. B., a woman, aged 56 years, was admitted to the hospital (to Dr. B. S. Oppenheimer's service) January 28, 1934. One year previous to her admission she had noted red blotches on the right side of her neck. These lesions were evanescent. However, during the last six months the blotches appeared more frequently, became more extensive, and spread to the left side of the neck, lower eyelids and trunk. They were dark red and irregular in shape. During the past two years she had noticed blood on her handkerchief on blowing her nose. About three months ago while eating she noticed a blue blister beneath her tongue which burst and bled for half an hour. She estimated the quantity of blood lost as about a cupful. There was marked anorexia, and the patient had lost 11 pounds in the four month period previous to admission. She had experienced attacks of precordial oppression and dyspnea on exertion. Palpitation was severe and frequent. She had had numbness of the fingers for the past two years, and for six months sensations of pins and needles in her fingers.

Examination showed a thin, gray-haired woman with cyanosis of the lips. There were arteriosclerotic changes in the vessels of the fundi. The uvula was swollen and ecchymotic, and there were numerous groups of large petechiae on the buccal mucosa, some of which had white centers. The chest was emphysematous and the dorsal spine kyphotic. The lungs were clear. The heart was normal except for frequent extrasystoles. The blood pressure was 140 systolic and 80 diastolic. The liver was

palpable to the umbilicus, and was unusually hard and firm. The spleen was enlarged to three fingers below the free costal border. On the left side of the neck, on the eyelids, and in the right groin there were large purpuric spots. There was no lymphadenopathy.

The hemoglobin was 80 per cent; red blood cells 5,000,000; platelets 230,000; white blood cells 12,000; polymorphonuclear neutrophils, 44 per cent; lymphocytes 54 per cent; monocytes 1 per cent and eosinophiles 1 per cent. The tourniquet test was negative. The brom-sulphthalein and galactose tolerance tests gave normal results. The urine on repeated examinations contained abundant albumin, a few white blood cells, hyaline casts, and on one occasion an amyloid cast. There was no Bence-Jones protein in the urine. Roentgenologic studies of the gastrointestinal tract failed to reveal any lesion. Roentgenograms of the chest showed only a hypertrophy of the left ventricle. Roentgenograms of the bones revealed no lesion. A Congo red test showed 100 per cent tissue absorption at the end of one hour. In view of the fact that no other cause for the symptoms was ascertainable, the diagnosis of primary generalized amyloidosis was made. While in the hospital she had repeated crops of cutaneous hemorrhages. On one occasion she had frank blood in the stool, and sigmoidoscopy revealed numerous petechial hemorrhages in the rectal and sigmoidal mucosa. The blood fibrinogen was 350 mg. The blood protein was 7.8 per cent, of which 4 per cent was albumin and 3.8 per cent globulin. The cholesterol was between 340 and 375. The Van den Bergh reactions were normal. The blood Wassermann test was negative. The sedimentation time was 23 minutes.

She was given liver extract intramuscularly, 2 c.c. twice a week. The patient left the hospital on March 7, 1934 and died three weeks later. Her private physician's diagnosis of the cause of death was "uremia."

Summary. A woman, aged 56 years, showed purpuric lesions of the skin and mucous membranes for one year. The liver and the spleen were considerably enlarged; there was marked albuminuria, a normal blood pressure, a normal blood protein with an elevated blood cholesterol. The diagnosis of amyloidosis was made and confirmed by the Congo red reaction which showed 100 per cent absorption.

Case 4. L. C., male, aged 38, admitted to the service of the late Dr. N. E. Brill, September 25, 1923. The family history was irrelevant. Twenty years before he had had a chancre and four years before a left-sided "pleurisy" which lasted two weeks. For 10 years he had had occasional frontal headaches. Five years prior to admission he noted dyspnea on exertion. This gradually increased and recently he had suffered from precordial pain when he hurried. About two months before admission his feet began to swell. For the past week he had had choking sensation, dyspnea and swelling of the abdomen. His ears had begun to discharge two months before entry to the hospital.

On examination he presented a diffuse anasarca with edema of the feet, hydrothorax and ascites. The heart was somewhat enlarged, with a short systolic murmur at the apex. The blood pressure was 160 systolic and 50 diastolic. The blood showed a moderate secondary anemia. The temperature was 100.2° F. and the pulse varied between 92 and 120. The knee jerks were absent. The urine contained abundant albumin and many hyaline casts. The blood urea nitrogen was 14 mg. per 100 c.c., cholesterol 170 mg., glucose 200 mg., and carbon dioxide 46.2 volumes per cent. The blood Wassermann test was negative. He died the day following admission in pulmonary edema.

Autopsy. The tracheo-bronchial lymph nodes were anthracotic. Both pleural sacs contained one liter clear fluid. The lungs showed edema and passive congestion. The pericardial cavity contained 100 c.c. of clear fluid. The musculature of the heart was dark brown and showed marked fatty changes. The mitral valve was thickened. The coronary arteries showed slight arteriosclerosis. The aorta showed a

few arteriosclerotic plaques in the arch and in the sinuses of Valsalva. The abdomen contained 1.5 liters of clear fluid. The liver was congested and fatty. The spleen was enlarged, deep red and showed an increase in fibrous tissue. The adrenals were normal. The pancreas was fibrotic. The kidneys were large, the capsules stripped easily and the cut surface was smooth and brown. The glomeruli were hardly visible. The microscopic examination showed passive congestion of the lung and liver, and diffuse amyloid change in the liver, spleen, kidneys and adrenals.

It seems rather strange in view of the frequency of chronic ulcerative colitis that amyloidosis has hitherto not been reported as a sequence, as in the following case.

Case 5. F. P., aged 48, was admitted to the service of Dr. B. S. Oppenheimer November 7, 1931 and died January 17, 1932. She gave a history of three operations for rectal stricture. Three months before admission her legs and abdomen began to swell.

The patient was emaciated and presented a large liver, a purulent discharge from the rectum and edema of the back and legs. The blood pressure was 134 systolic and 80 diastolic. The hemoglobin was 48 per cent, red blood cells 2,650,000, white blood cells 2,600, of which 77 per cent were polymorphonuclears. The urine contained large amounts of albumin. The stools gave a strongly positive test with guaiac. The Congo red test showed a retention of 29 per cent. The blood urea was 14 mg., the blood glucose 75 mg., the cholesterol 165 mg. per 100 c.c. The blood Wassermann test was negative. The blood serum proteins were 4.6 gm. of which the albumin fraction was 2 and the globulin 2.6 gm. Sigmoidoscopy revealed a granulomatous mass involving the lower rectum and the anus; the posterior vaginal wall was also involved. The remainder of the gastrointestinal tract was normal by roentgen-ray. The chest was normal. A barium enema revealed marked constriction of the mid-sigmoid with fistulous communication between the sigmoid and ileum. A colostomy was performed but the patient continued to fail and she died a short while thereafter.

Anatomical diagnosis. Chronic ulcerative stenosing proctitis with multiple fistulae, chronic sigmoiditis and colitis (descending colon), chronic cystitis, terminal ileitis. Amyloidosis of the kidneys. Dilatation of the right auricle and ventricle; broncho-pneumonia of the left upper lobe. Thrombosis of the left pulmonary artery; chronic infectious swelling of the spleen. Pyelonephritis. Hydrothorax. Perihepatitis and perisplenitis. Organizing emboli of left pulmonary artery, pulmonary infarct.

Summary. A woman of 48, with a long standing chronic colitis and terminal ileitis with multiple intestinal fistulae, who developed a nephrotic syndrome caused by renal amyloidosis. The Congo red test showed a retention of the dye within the normal range, proving that the test is not infallible. The amyloidosis was limited to the kidney.

Case 6. A woman, aged 23, admitted to the service of Dr. G. Baehr, had an ileostomy performed seven years before for ulcerative colitis. Following this she was readmitted to the hospital on several occasions; once for intestinal obstruction with nausea and vomiting which subsided within several days and once with an ischio-rectal abscess which was incised and drained and which continued to drain up to the time of admission. She had also developed a recto-vaginal fistula and a peri-rectal abscess. The ileostomy functioned well and she was able to carry on a somewhat restricted life. One year before this admission she vomited about once a month. The vomiting was accompanied by mild abdominal discomfort and was not profuse. Her last bout of vomiting occurred two weeks before admission. Nine days before admission she noted oliguria and two days later complete anuria. At that time she began to vomit profusely and continued to vomit until the time of admission. Head-

aches and dizziness accompanied this spell of vomiting. Physical examination showed a poorly developed, poorly nourished female, appearing acutely ill. The breath was uriferous. The heart sounds were of fair quality. The blood pressure was 90 systolic and 70 diastolic. An ileostomy of the right lower quadrant, apparently functioning well, was present. There was an anal stricture not admitting the examining finger. There were discharging granulating ulcerations of the right inguinal and right ischio-rectal regions. The extremities were cold and clammy. There was a positive Chvostek sign. The hemoglobin was 36 per cent; red blood cells 2,100,000; white blood cells 7,200. Her urine showed abundant albumin and innumerable casts. The urea nitrogen on admission was 178 mg.; calcium 6.3 mg.; phosphorus 7.7 mg.; chlorides 350 mg. per 100 c.c. The CO_2 49.5 volumes per cent. The electrocardiogram showed sinus tachycardia with tendency to left ventricular preponderance. The sedimentation time was 7 minutes. The phenolsulphonephthalein test showed no excretion. Scrapings from the fistulae showed no evidence of tuberculosis. The fundi were normal. The von Pirquet test was negative. The Mantoux test was positive with a 1/1000 dilution. A concentration test of the urine showed a maximum concentration of 1.012. The patient was given intravenous glucose and saline solution, and calcium gluconate. Her urinary output gradually increased, signs of tetany subsided, the blood urea gradually fell to 70 mg. per 100 c.c. Her blood chlorides rose to 550 mg.; calcium rose to 10.4 mg.; phosphorus fell to 4.3 mg.; the total protein was 6.3 per cent; albumin 2.3 per cent; globulin 3.1 per cent. Her urine, however, continued to show abundant albumin with occasional hyalin and granular casts and many leukocytes. Her blood pressure ranged from 64 systolic and 48 diastolic to 86 systolic and 46 diastolic.

The Congo red test showed 100 per cent retention on one occasion and 95 per cent retention on another occasion. In retrospect the clinical picture was explained on the basis of a long standing chronic oliguria with associated nitrogen retention producing vomiting from time to time and finally reaching such a stage that vomiting became continuous with resulting anuria. A vicious cycle by loss of chlorides caused an extreme azotemia with peripheral collapse.

Whether or not an intercurrent glomerulonephritis was present is merely conjectural. The urine was free of lead and arsenic. The patient was given liver extract and a transfusion. There was a moderate improvement in her general condition, and she was discharged from the hospital one month after admission.

THE MECHANISM INVOLVED IN THE PRODUCTION OF AMYLOIDOSIS

Experimental Amyloidosis. In what manner do suppuration and tissue necrosis bring about the production of amyloid substance in the mesenchyme? Some light has been thrown upon the problem by the successful experimental production of amyloid. Credit for the first valid experimental production of amyloidosis belongs to Kuczynski²⁰ who in 1922 produced amyloid disease by the injection of 5 per cent sodium caseinate over prolonged periods into mice; he also found that it could be produced by excessive feeding of such protein. Since then Kuczynski's work has been repeatedly confirmed, especially by Smetana,²¹ Jaffé,²² Lucké, Letterer,²³ and Grayzel, Jacobi and Warshall.²⁴ Jaffé carried on his work on an extensive scale. He employed a 3 per cent solution of sodium caseinate in normal sodium chloride solution injected into mice every few days. After the sixtieth injection the results were uniform, so that he could always find amyloid in the spleen. After the eightieth injection the amyloid was

distributed in most of the parenchymatous organs, i.e. the spleen, the liver, the kidneys, suprarenal glands, the lymph glands and the intestines. Eventually every organ was affected except the skin and the central nervous system. He obtained the same results by the repeated injections of sterile human serum so that he regards amyloidosis as due to chronic protein poisoning. Jaffé and others have found a crystalline form of amyloid in experimental animals which apparently is only rarely found in human amyloidosis. He found that the blood of his experimental animals showed a normal refractometer index and a normal hydrogen-ion concentration.

Grayzel, Jacobi and Warshall found that diet influenced the production of amyloidosis. An adequate diet but one containing an abundance of vitamins A and B will retard the development of experimental amyloidosis. They also noted the resorption of amyloid in animals in the early stages if powdered whole liver was added to the diet. No resorption was noted in the advanced stages. It is upon these observations that the treatment of amyloidosis by liver is based.

Letterer produced amyloid not only with sodium caseinate, but with gelatine, egg albumin, cereal albumin, nuclein and peptone. He also implanted portions of normal spleen and kidneys and occasionally obtained amyloidosis. Occasionally he produced amyloid with injections of selenium, especially if the animals were fed little water. The ingestion of water seemed to have an influence on the production of amyloid even with sodium caseinate injections; water restricted animals required a much smaller dose than those who were given water freely.

In this connection, the findings of Doerken and Arndt²⁵ are pertinent. They studied the incidence and histological reactions of amyloid in 100 horses employed in the production of antitoxin. They found that 60 per cent of these animals showed amyloidosis, and the incidence of affection of the various organs parallels closely those observed in human and experimental amyloidosis. The animals had been used for the production of different varieties of antisera for two and a half to 54 months. Before the eighth month, amyloidosis was never found, after the sixteenth month nearly always and after the twenty-first month always. Curiously, the horses employed for the production of scarlet fever antisera showed a greater incidence of amyloidosis than those used for productions of tetanus or diphtheria antitoxins. Unfortunately no observations upon the total protein content of the blood of these horses were made, but it is interesting to note, as upholding Letterer's contention, that hyperglobulinemia is the direct cause of amyloidosis, that Reitstötter²⁶ found in serum treated horses an increase of globulin, sometimes up to 100 per cent at the expense of the albumin fraction.

The changes noted by many observers in the blood protein when protein is added to the body economy either parenterally or otherwise are significant. Moll²⁷ found an increase of globulins in the blood after repeated injections of protein gelatin and killed bacteria. Rowe²⁸ found an increase in blood

proteins on a continued high protein diet, and Doerr and Berger²⁹ observed high blood proteins in rabbits repeatedly injected with horse serum; Berger³⁰ found that this increase is at the expense of the albumin with a corresponding rise in the globulin fraction. In his experimental animals, Letterer found only a slight increase in the total blood and globulin protein.

Clinically a hyperproteinemia has been found but rarely in generalized amyloidosis. Koref³¹ in a case of amyloidosis secondary to tuberculosis found the blood proteins 10.89 gm. per 100 c.c. with an albumin-globulin ratio of 20:80. There was a slight rise in the total fibrinogen. These figures are remarkable in view of the fact that in this case there was a free proteinuria. Petschacher³² found hyperproteinemia and hyperglobulinemia in a case of amyloidosis consequent to an ulcerating tuberculosis.

As another link in the chain of his evidence, Letterer found that there is a close affinity in the molecular content of carbon, hydrogen, nitrogen and sulphur atoms between amyloid and globulin.

Until systematic studies of the blood proteins in human and experimental amyloidosis have been made, all that can be said for Letterer's contention is that it is highly suggestive. The fact that low blood proteins are found frequently in human amyloidosis does not invalidate his views because it may easily be conceived that when the amyloidosis is so far advanced as to involve the kidneys and cause proteinuria, a previously high proteinemia may be converted into a deficiency. As far as our present knowledge permits us to say the only conditions in which a hyperproteinemia and hyperglobulinemia are found with any degree of consistency are dehydration and multiple myeloma (Perlzweig, Delrue and Geschicker,³³ Shirer, Duncan and Haden³⁴). This latter observation made since Letterer's publication adds strong support to his contention.

DIAGNOSIS

If we may judge from the results of experimental amyloidosis in mice and the observations upon horses treated for the production of antisera, amyloidosis is insidious, and does not make itself clinically manifest in man until the suppurative focus has been in existence for many months. According to Waldenström,³⁵ it requires one to two years before the amyloid becomes deposited. Inasmuch as the spleen is the first organ and the one most consistently involved, enlargement of that organ is probably the first sign. As a rule, the clinician observes the patient when the disease has already spread to other viscera, especially the liver and the kidneys. Involvement of the liver never gives rise to gross evidences of hepatic insufficiency, but manifests itself clinically merely in enlargement of the organ. Sometimes the enlargement is extreme as in the case clinically reported by Rachmielowitz³⁶ where it reached nearly to Poupart's ligament. The dominant clinical manifestations of generalized amyloidosis arise from involvement of the kidney, and indeed, most recent reports on the clinical

aspects of amyloidosis are concerned only with the renal manifestations under the title "amyloid nephrosis." We regard the term "nephrosis" as unfortunate for many reasons: (1) Because under no circumstance is the amyloid kidney a pure epithelial involvement of the kidney according to the definition under which the term nephrosis was first coined, but always represents involvement of the connective tissue and vascular structures; (2) Because clinically the renal manifestations do not always correspond to the conventional criteria of nephrosis formulated by Epstein and others but are frequently accompanied by vascular reactions of which hypertension and azotemia are the prominent expressions; (3) Because in the light of modern studies, "nephrosis" is not a disease but a symptom complex whose clinical manifestations are the result of a hypoproteinemia from whatever cause. The term nephrosis, therefore, if used at all should be applied to losses of protein sustained by way of the kidney.

Albuminuria is the most constant symptom of generalized amyloidosis; it varies from a trace to many grams per liter. As a rule albuminuria signifies involvement of the glomeruli by amyloid, but not necessarily so (Rosenblatt). On the other hand, amyloid infiltration of the kidney is not always accompanied by albuminuria. When the albuminuria becomes excessive (more than 1 gram per liter) the typical secondary evidences of hypoproteinemia become manifest with anemia, edema, anasarca, cholesterinemia and doubly refractive lipoids in the urine (Rachmielowitz, Shapiro,³⁷ Noble and Major,³⁸ Bannick, Berkman and Beaver,³⁹ Rosenblatt¹⁵). Sometimes the cholesterol in the blood reaches excessive figures; in the case reported by Rachmielowitz, 625 mg. per 100 c.c. of blood.

In the majority of instances the systemic blood pressure in generalized amyloidosis is low. Indeed Rosenblatt, in his large series, found no instance in which the pressure was over 140 mm. of mercury. On the other hand, hypertension has been observed by numerous observers (Volhard and Fahr,⁴⁰ Bell,¹⁸ Noble and Major, Dixon). Sometimes the hypertension develops as a terminal event. In the case reported by Gerber (reported previously during the lifetime of the individual by Rachmielowitz) the tension rose two and a half years after the first observation. Perla and Gross report a similar observation in a patient 16 years of age. The majority of observers associate hypertension with the onset of secondary renal contraction (Noble and Major).

Azotemia has been reported frequently. In Dixon's series it was present in 26 per cent of the cases; it is apparently independent of the systemic blood pressure, even causing death with a normal or low tension (Bannick, Berkman and Beaver), thus differing from the usual association witnessed in the primary or secondary contracted kidney.

A not infrequent symptom of amyloidosis is purpura. It was present in one of my cases (Case 2) and has been reported by Königstein,⁹ Perla and Gross,¹⁹ Leupold⁴¹ and Strauss.⁴² Strauss reports amyloid involvement of the blood vessels of the skin in the purpuric areas.

Since the introduction of the Congo red test (Bennhold ⁴³) the diagnosis of generalized amyloidosis has been placed on a sounder footing. This test depends upon the disappearance of the dye after intravenous injection of the dye. Melamed,⁴⁴ whose experience in Montefiore Hospital with the test has been extensive, regards the diagnosis of amyloidosis as justified when the retention of the dye is 50 per cent or over, doubtful when it is between 25 per cent and 50 per cent and negative when it is below 25 per cent. A retention of 100 per cent makes the diagnosis certain. Kramer and Som ⁴⁵ found vital staining with intravenous Congo red of definite aid in outlining the borders of a localized amyloid tumor of the larynx. Gerber noted the persistence of the dye in the affected organs years after the Congo red test had been performed.

IS AMYLOIDOSIS REVERSIBLE?

This question is obviously important. Gardner ⁴⁶ in 1891 reports the case of a man with extensive necrosis of the femur with all the constitutional evidences of amyloid disease: albuminuria, enlarged liver and cachexia. After amputation of the leg, the patient recovered completely. Walker ⁴⁷ reports the case of a boy aged four, who two years after the onset of a chronic empyema developed albuminuria, enlarged liver and spleen and cachexia. A thoracoplasty was performed. One year later the liver and the spleen had diminished appreciably in size and the cachexia improved. Eight years later the boy was completely well. Waldenström,^{35, 48} in two publications, reports numerous biopsies of the liver upon suspected cases of amyloidosis and in three instances found complete disappearance of the amyloid after healing of a suppurative tuberculous focus. Incidentally he notes that a liver may not be enlarged and yet show considerable amyloid. Métraux ⁴⁹ reports an extremely interesting observation. A child of 13 developed typical amyloid disease the result of a chronic osteomyelitis. The Congo red test was positive. The osteomyelitis healed, and five years later the Congo red test had become negative, the albuminuria had disappeared, and the liver had returned to normal size. Two years later the osteomyelitis recurred and three weeks later the patient died from sepsis. The liver showed amyloid with healing granulomatous changes, the Küpfer cells contained amyloid and the kidneys showed beginning contraction. It is doubtful whether the amyloid recurred after only three weeks' suppuration so that we must assume in Métraux's case the patient was clinically but not anatomically healed.

Recently Reimann ⁵⁰ reports the case of a woman, aged 30, who developed amyloid disease two years after the first symptoms of tuberculosis and one year after a thoracoplasty. The Bennhold test showed complete disappearance of the dye after one hour. The patient slowly improved, and nine months later only a normal per cent of the dye was retained. All symptoms of amyloidosis eventually disappeared and three years later the

patient was perfectly well. The liver and the spleen were not palpable and the urine contained only a trace of albumin.

In experimental amyloidosis Kuczynski noted resorption of the amyloid if the lesion were not too advanced. Morgenstern also noted that amyloid deposits began to subside after stopping the injections of nutrose and at the end of four months had practically disappeared. In the liver he noted some connective tissue replacement. Grayzel, Jacobi and Warshall also noted resorption of amyloid in animals in the earliest stages of the process and especially if liver was added to the diet. No regression was noted in the advanced stages.

In summary one can conclude that the clinical regression of amyloidosis is possible provided the focus is removed. Whether complete anatomical healing with *restitutio ad integrum* is possible remains doubtful.

ATYPICAL AMYLOIDOSIS

This term was employed by Lubarsch to connote instances of amyloidosis in unusual sites and without apparent cause. There is usually no involvement of the liver and spleen, while such organs as the heart and lungs, the skin and striated muscles are particularly involved. Sometimes the amyloid occurs as tumor-like masses, either of pure amyloid or as a secondary involvement of a new growth (usually a myeloma). Frequently, the usual colorimetric reactions of amyloid are absent.

Lubarsch reported three cases. In the first, amyloid was deposited in the heart, lungs, stomach, esophagus, the intestines and the skin. In the second, the patient had signs of scleroderma and myotonia and a large tumor of the tongue which proved to be a massive deposit of amyloid. In the third, there was marked amyloidosis of the stomach, lungs, heart, spleen, trachea, the entire genital tract and the bronchial and mesenteric lymph nodes. Gerstel⁵¹ reports another case of huge amyloidosis of the tongue, with amyloid deposits in the skin of the neck, the gastrointestinal tract, the heart and the blood vessels. Pick⁷ reports two cases. The first, a man aged 54, had difficulty in swallowing and a generalized disturbance in muscular function. A diagnosis of myotonia, scleroderma and carcinoma of the tongue was made. Autopsy revealed a widespread amyloidosis of the muscles, the tongue, the heart, stomach, intestines, lungs and serous membranes. The second was a woman aged 51 with swelling of the tongue and muscles of the neck and thickening of the cervical skin. At autopsy there was found a diffuse amyloidosis of the tongue, the floor of the mouth, soft palate, pharynx, esophagus, stomach, intestines and diaphragm. In neither case was a cause discoverable. Recently Warren reports a case of general involvement of the musculature without involvement of the parenchymatous organs. Mollow and Lebell⁵² report the case of a man aged 60 who clinically showed hypertonia of the muscles, enlargement of the tongue, and abdominal pain. At autopsy generalized amyloidosis of the muscles and skin

was found, without involvement of the parenchymatous organs. Perla and Gross report three cases. The first was a female, 53 years of age, with extensive amyloid disease of the heart, tongue, gastrointestinal tract and other organs, who died of congestive heart failure. The second was a female aged 16 years, with extensive amyloid deposits in the kidneys, liver and suprarenals, who died in uremia. She had an ankylosis of one joint. The third case was a female, 63 years of age, with amyloid contracted kidneys who died in uremia. She had severe coronary sclerosis and a healed infarction of the left ventricle. The amyloid was limited to the kidneys. Strauss reports the case of a man, aged 72, who had dyspnea and generalized enlargement of the lymph nodes. The amyloid was found in the epi- and pericardium, lungs, lymph nodes, adipose tissue. There was a massive involvement of the muscle-free blood vessels. He discusses 28 previously reported cases of atypical amyloidosis and suggests the name para-amyloidosis to comprise these bizarre forms.

Herxheimer and Reinhart⁵³ collected 38 cases of amyloidosis of the upper respiratory tract and lung and eight cases of amyloidosis of the lung. They hold that no sharp distinction can be made between the generalized and localized forms of amyloidosis, because one may find the most extraordinary combinations.

In the atypical variety may be mentioned the tumor-like masses found in the upper respiratory tract cited by Pollak⁵⁴ and Kramer and Som.

Lubarsch has attempted to classify these atypical cases of amyloid disease into three groups: (1) Those involving mainly the skin simulating scleroderma; (2) Those in which the dominant infiltration is in the muscle simulating myotonia; (3) Those involving the tongue simulating neoplasm. In addition we would add a fourth, namely, cases of amyloidosis associated with chronic deforming arthritis. This seems the best clinical classification of so-called atypical amyloidosis at present at our disposal, but it is by no means to be considered inclusive.

SUMMARY

The chemical nature of the amyloid substance is not conclusively known. Pathologically, amyloidosis usually represents an involvement of the reticulo-endothelial system and the pericapillary and periglandular connective tissue. Almost any tissue except the cerebrospinal substance may be involved, with a special predilection for the muscles and skin. In addition to the conventionally known causes, such as tuberculosis, chronic suppuration, syphilis, Hodgkin's disease and necrotizing blastomata, amyloidosis, either general or localized, is frequently associated with multiple myeloma and its attendant Bence-Jones proteinuria and with ulcerative lesions of the bowels. A case of amyloidosis associated with chronic deforming arthritis is reported. Such an association has been reported not infrequently, though the relationship is not clear. The number of reported cases of amyloidosis

without apparent cause, in other words, primary amyloidosis, is progressively increasing and constitutes an important nosological entity. Experimentally, amyloidosis has been produced in various ways, but the underlying principle represents a prolonged overdosage with protein, preferably by the parenteral route. The evidences in favor of Letterer's contention that amyloidosis is the result of a hyperproteinemia and an associated hyperglobulinemia are reviewed and may be regarded as highly suggestive.

The clinical diagnosis of amyloidosis is dependent upon the following signs: (1) The enlargement of the viscera that may become palpable, namely the spleen and the liver. (2) The development of signs of the so-called nephrotic, but better termed hypoproteinemic syndrome consequent upon the involvement of the kidney. These are proteinuria, diminished blood proteins, hypercholesterinemia and generalized anasarca. In later stages, general arterial hypertension and azotemia may develop. The latter may occur without a co-existing hypertension, in contradistinction to other varieties of renal disease associated with hypertension. (3) Purpura of the skin. This sign has been less commonly observed but has been reported sufficiently frequently to be regarded as a symptom of the disease. (4) The Bennhold Congo red test forms the most important confirmatory test of amyloidosis. A 100 per cent retention of the dye is diagnostic.

There is abundant evidence that amyloidosis is clinically reversible; whether it is anatomically reversible has as yet not been definitely proved. Atypical amyloidosis constitutes a diverse variety of anatomical lesions. Clinically they may thus far be classified into four groups: (1) cases simulating scleroderma; (2) cases simulating myotonia; (3) cases simulating tumor of the tongue; (4) those associated with deforming arthritis.

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ADEQUATE TESTS OF CURATIVE THERAPY IN MAN*

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It is widely recognized that the subject of therapeutics has a great emotional appeal for the layman, and as a corrective measure a clear view of therapeutic possibilities is expected of the physician. But it is on the subject of therapy that the demands of practice strain the exercise of cool judgment to the utmost. The doctor may adopt either an exaggerated skepticism, or an exaggerated optimism, depending on his temperament. He is also nearly always subject to fashions in the use of certain popular methods of treatment. Due to such influences, no doubt, the element of belief as distinguished from objective data plays a large part in determining the physician's attitude toward therapeutic problems. A question that is often asked when therapeutic practice is discussed illustrates this dependence on belief: One physician asks another "Would you demand such treatment for yourself in case you were ill?" This question implies a consideration of the safety and freedom from discomfort of the therapy, but its main object is obviously to pierce beyond any facts and find the state of belief of the person who is quizzed. The profession is thus quite practical but not entirely rational when questions of therapeutic efficiency are concerned. This irrational approach persists today in spite of the fact that it has been repeatedly shown that it is possible to measure the effectiveness of curative therapy. In this paper the data accumulated in support of the value of several well known curative agents are reviewed and the experiments are cited as examples of effective methods for testing therapeutic agents. Such a discussion is not to be found in the recent medical literature. It is hoped that it will aid in defining standards of achievement for those who advocate new cures, and also contribute to a better reasoned attitude by the profession when they are confronted with reports of therapeutic success.

During the introduction of quinine, of diphtheria antitoxin, and of insulin, testing methods ranging from the most primitive to the most exact were devised and used. The experiences with these three medicaments furnish good examples of the various types of clinical therapeutic experiments that have proved most useful.

The possibility of curative therapy specific for a given disease was first demonstrated satisfactorily in the case of quinine¹ introduced to Europe in 1638. It was introduced in the form of various preparations of Peruvian Bark, in the same way that many other products of vegetable origin were made known to the medical profession in the seventeenth century. Reports of single cases or "cures" that resemble testimonials were recorded. The

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"cures" seem to have derived much of their importance as a result of the rank of the persons treated; for example, it is related that a provincial governor of Coreggidor was successfully treated, later the Countess of Chin Chon, and finally in 1649 the future Louis XIV of France. The Jesuits adopted the bark and distributed it widely. It was also sold by drug dealers. Because there was little curiosity in Europe as to its source, and because the Indians who gathered it for market did not believe that it had any potency as a medicine, a good deal of adulteration and substitution occurred.

Opinion was divided as to its value for thirty to forty years. During this time and also later, the preparations of the drug frequently lacked potency. Certain prejudices of the time such as those resulting from the prevailing theories of disease processes, and from the religious character of some of the drug's supporters (as the Jesuits) prevented an impartial judgment. In 1676, Sydenham gave an account of the use of Peruvian Bark that was of a different character.² He related his observations on the use of the Bark over a period of years. He described the type of fever, namely the remittent fever, in which it was useful, the symptomatic results, and by considering dosage explained the tendency to relapse observed by others. The dosage that he recommended was quite similar to that in use today. This publication no doubt had some direct effect upon the adoption of the drug, but it was not as influential as the activities of Talbor who popularized its use as part of a secret formula which was published after his death by Louis XIV. The disclosure that Peruvian Bark formed the potent part of this formula apparently fixed its value until the present time. Much has since been learned about Peruvian Bark: The active principle was isolated in 1821, and the parasite of malaria was recognized by Laveran in 1880; but these and other facts of lesser importance have not materially altered our views in regard to its therapeutic application.

The vicissitudes of quinine from the time it was first called to the attention of Europeans until it was finally accepted are duplicated in many respects in therapeutic efforts today. Remedies are sometimes used and advocated by lay persons, medical sects, and by physicians, in the treatment of ill-defined groups of diseases, with no rational explanation of the results expected. Data may be presented in support of such claims that have no more value than a testimonial. The customary reaction to such claims is the setting up of a group that believes, and a group that does not believe, and these cannot reconcile their differences until impartial experiment determines the truth so it can be seen by all.

Sydenham's contribution to the methods of observing therapy was of the greatest importance. He showed that a skillful clinician with a knowledge of the course of a given disease, derived from experience, could observe the effects of medication and come to a valid conclusion as to its worth. This method is within the daily activity of every active and skillful clinician. It has been used more widely than any other, but the results have often been unsatisfactory. It is almost impossible to draw the boundary line between

skillful observation and the unconsciously colored reports of those who favor belief or disbelief. The personal integrity and skill of the individual author cannot be known to all of us, and without this knowledge reports of observations of symptoms as serially observed in practice cannot be evaluated. As a result, and due to the combined efforts of a long succession of physicians, improved ways of testing medicaments have been devised.

The development of further specifics such as diphtheria antitoxin dominated medical thought and progress during the isolation of many bacterial agents and the beginning of immunology in the late nineteenth and early twentieth century. The infectious theory of disease was leading to active search for curative methods in a fruitful direction. Experimental medicine was active and productive.

The steps through which diphtheria antitoxin came to the attention of the profession were as follows.³ Löffler in his description of the diphtheria bacillus noted that although it did not invade the body it produced general systemic and distant toxic effects. Roux and Yersin in 1889 showed the presence of a soluble toxin by inoculating animals with broth from which the bacterial bodies had been separated by means of porcelain filters. Von Behring, Wernicke and Futaki showed that the blood serum of inoculated animals and those recovering from the disease neutralized the effect of such toxins when passively administered in other animals. In the years 1890, 1891 and 1892 these authors described the production of such antibodies in horses, sheep and cattle, and gave methods of estimating their potency in guinea pigs. During the course of these studies, the application of this knowledge of antibodies to the cure of disease in man was kept in mind, and at Christmas time in 1891, the first child was given 50 c.c. of sheep antitoxic serum subcutaneously in the von Bergmann Clinic with a satisfactory result as reported by von Behring and Wernicke. More extensive clinical trials were made in 1892 and 1893, and the antitoxin was supplied to others and widely used after 1894.

No therapeutic measure so well tested in animals had ever before been given to clinicians for use in patients, and the lesson of the worth of carefully controlled observations led to a conscious effort to conduct clinical tests in a similar manner. Symptomatic results from antitoxin sufficiently striking to form the basis of a report like Sydenham's report on Peruvian Bark, were apparent when only a few patients had been observed. The membrane was found almost invariably to cease spreading, and to disappear, together with general improvement. The number of cases treated and described in written reports was enormous. Two new features of these reports are noted: (1) The adoption of simple statistical methods such as averages, tables and graphs to describe the effect of therapy on symptoms, on the incidence of complications and on the death rate. (2) The comparison, wherever possible, of these findings with those of control series of cases. It was widely felt that observations on large numbers of cases were better than observations on small numbers of cases because the variability of

the disease was a relatively smaller source of error in the larger series. As control series for comparison, nearly all workers used groups of patients seen in the years immediately before 1894, the year in which the general use of diphtheria antitoxin was begun.

It seemed to many that these data gathered on this unprecedented scale, and according to methods that were new in part, did not constitute an improvement over the simpler and easier studies of Sydenham. A good many criticisms were made.⁴ Most of these were concerned with the suitability of the controls seen previous to 1894 with which treated cases were compared. It was pointed out that all the cases reported were seen in hospitals, and that the character of the hospitalized cases might conceivably change from time to time due to variations in the criteria for hospitalization. Further studies outside the hospitals disposed of this objection. It was further pointed out that the treated series were diagnosed by means of throat culture, but that control cases were not so diagnosed. Analyses showed that only very small errors could arise from this source. A more serious objection to the use of controls observed before 1894 was raised by epidemiological studies. Within a few years before or after 1894 a severe world wide epidemic of diphtheria came to an end, without any relationship to the introduction of antitoxin as a therapeutic agent. The number of cases fell off rapidly, and the proportion of fatalities among the remaining cases also became less. A false idea of the effectiveness of the serum therapy had thus been gained from comparisons between cases seen before and after the termination of this epidemic. The great importance of studies in which the control observations were adequate was then acknowledged. In the best of these, by Fibiger, in Blegdam's Hospital two groups of patients were observed simultaneously in the same hospital, and chosen by means of numbers assigned impartially on entrance. In two other experiments the results of treatment were compared in two similar, but separate hospitals at the same time, in the same city, in Berlin at the Charité and the Bethanien Hospitals, and in Paris by Roux, Martin and Chaillou. Since such statistical studies of death rates are the material that is now quoted in support of this important medication, a table is given which indicates the results of several representative experiments, the first with the inadequate controls, the other three those just described.

TABLE I

Mortality Rate of Diphtheria Cases Treated with Antitoxin Compared with Cases Treated without Antitoxin

Reference	With Antitoxin			Without Antitoxin		
	Number	Number Died	Per cent Died	Number	Number Died	Per cent Died
New York ⁵	56,425	8,464	15.0	27,210	8,496	34.9
Paris ⁶	448	11	24.5	520	312	60.0
Berlin ⁷	317	53	16.7	260	102	43.1
Copenhagen ⁸	239	8	3.5	245	31	12.5

The initial venture of modern medicine into therapeutics was thus accomplished in a scientific manner. The actions and potency of diphtheria antitoxin were first carefully ascertained in animals. From these experiments the dosage of the antitoxin was easily controlled. The observation of the action of antitoxin in a consecutive series of cases according to the simple technic that Sydenham employed played a large part in its wide adoption. For written reports, however, statistical methods came into play. These gave results that were much too favorable, due to the fact that epidemic fluctuations were not observed, but the three experiments quoted above appear to have been adequately controlled. The data quoted in the above table have withstood the criticism of several critical generations.

As other therapeutic sera have been developed the same methods have been used to ascertain their usefulness in man. New variations in the application of the statistical method were often required. Antimeningococcic serum was used on a large scale first in the epidemic of 1911, and 1912, with a mortality rate (30.9 per cent) much below that always previously reported (50 per cent to 80 per cent).⁹ Since that time results have been found satisfactory by many, especially by those who have paid particular attention to the use of serum possessing the necessary type specific antibodies (Wadsworth, mortality rate 17.8 per cent).¹⁰ Dissatisfaction has been reported repeatedly by physicians who happened to see some marked variation from the average death rate in a small experience or by physicians who observed an epidemic in which the serum was not effective. It is unfortunate that no well selected series of control cases was compared with those treated with serum, as McCoy,¹¹ and more recently, Petrie¹² have pointed out. Those who have had definitely unfavorable experiences have possibly been given greater importance than they deserved. Petrie outlines the control methods that would be required for collecting the best data as follows: (1) A group of patients treated with serum. (2) A group of patients treated with frequent lumbar spinal drainage and (3) A group of patients treated intraspinally with normal non-immune horse serum. (4) A group of patients treated expectantly.

The serum treatment of lobar pneumonia may be divided into two periods in regard to the methods of testing employed. Before 1904 antipneumococcic sera were prepared without respect to the serologic differentiation among the pneumococci, and were used in small groups of cases by a large number of practitioners. The results were collected¹³ and the total was reported in statistical tables, together with each author's descriptions of the symptomatic results but with no thought of controls. The reports were favorable, but were not taken seriously, and as commonly happens with therapeutic procedures that are not definitely proved to be effective, the procedure fell into disuse, without the production of any evidence that could be shown to be unfavorable. Type specific antipneumococcic serum was shown to be clinically useful first by Cole,¹⁴ who observed a series of patients accurately after the method of Sydenham, and, due to the known excellent

character of his ability and experience, these results were accepted by many, despite the lack of adequate controls. Others,^{15, 16, 17, 18} have made great efforts to compare treated patients with controls in the same hospital during the same season. In one instance¹⁹ a direct comparison was undertaken between non-specific and specific horse serum concentrates. These results, expressed by means of tables of figures, are probably the most extensive and clear of any such therapeutic investigations.

In the case of scarlet fever antitoxin the symptomatic effects were observed repeatedly^{20, 21} and were compared with adequate controls, but the naturally low death and complication rates prevented the collection of the best kind of comparable data as to its therapeutic efficiency. A further clinical experiment was conducted by Blake and Trask²² that deserves special comment from the point of view of the methods of investigation employed. The clear rationale that had been provided for the use and actions of scarlet fever streptococcic antitoxin by means of the Schultz Charlton test and Dick test led Blake to inquire not only "Does the serum cure the disease?", but "Does the serum neutralize the toxin that is present and simultaneously cure the disease?" He was able to show by doing skin and neutralization tests with the sera taken at different stages of scarlet fever from 133 patients that toxin circulated in the blood stream during the time of greatest toxicity, that the toxic action of such blood was prevented by the administration of antitoxin, and that the neutralization of the toxic action of the patient's serum was followed by clinical cure of the disease. This method is applicable only where something of the action of the medicament is understood, and some essential feature of the disease can be made the object of measurement. Claude Bernard²³ early contrasted such rational experimental study of therapy in man and animals with statistical methods, presenting an array of objections to observations that were applicable to the mystical "average case." Therapeutic investigations in man such as Claude Bernard urged became of importance as the knowledge of physiology accumulated.

The most important developments in therapeutics in the recent past have been in the field of physiology as applied to medicine; by the replacement of hormones and vitamins lacking in disease. Insulin was the first of these. The methods through which its use became established are typical.²⁴

A large number of workers had confirmed and accepted Minkowski's explanation that the pancreas elaborated a hormone necessary to the metabolism of glucose. Diabetes was reproduced in the dog and carefully compared with diabetes in man. The disturbance in carbohydrate metabolism was measured by means of urinary and blood sugar, and the respiratory quotient. The discovery of Banting and Best, that watery extract of the pancreas maintained depancreatized dogs and lowered the blood sugar of rabbits, was the culmination of an extensive series of experiments by others which indicated that such a substance was present. Its application to man was a foregone conclusion. The preparation of extracts sufficiently non-toxic to be safe proved a temporary stumbling block, but this difficulty was

solved with the aid of Collip. Once a suitable concentration of the material was obtained and administered, observations of the carbohydrate metabolism showed that profound changes had been secured. Confirmation of these findings by others was all that was required to make obvious the effectiveness of the medicament. Subsequent analyses of series of such treated cases have been made with the purpose of clinical description and only incidentally to confirm the fact apparent to all that insulin is a specific remedy for diabetes mellitus. Such methods mark a definite step forward because the demonstration is conclusive and the information is not statistical. It is applicable to individual cases instead of the average case. The basis upon which such data may be developed is a clear conception of the nature of the disease.

When this search for trustworthy methods of testing therapeutic efficiency was begun it was hoped that experiments could be classified into various kinds. This has been done. Three different types of testing methods were distinguished as follows:

1. Observation of consecutive cases and comparison with the fund of experience (Sydenham).
2. Counting of cases, preparation of statistics, and comparison with similarly prepared controls (Louis).
3. Observation of the effect of medication upon some of the essential features of disease (Claude Bernard).

Outstanding successful examples of the application of each of these methods are described above. It was also hoped originally that the usefulness of each of these methods could be determined objectively from the reports in the literature. A tabulation was projected to show the results of different methods applied to the same therapeutic measure, in which only subjects about which general agreement had been obtained were to be included, with attention to the successful demonstration of the absence of effect as well as the presence of effect. Such comparisons were found to be impractical because the data were not adequate. There was a tendency for only one method to be used for each therapeutic agent, and carefully prepared reports of the lack of effect of therapeutic agents were very rare.

The statistical method is the only one of these three methods that has been the object of frequent discussion from the point of view of methodology. There are those who regard the statistical method, so called, most highly. There are others who place very little reliance upon information obtained in this way. The method in principle as Louis stated it²⁵ is quite simple. "For true experiences in medicine as I have elsewhere remarked (and as anyone may be convinced by what has preceded), true experience in medicine can result only from the exact analysis of numerous parts, well ascertained, classed according to their resemblance, compared with care, and counted." The mathematical manipulations that are useful in therapeutic experiments are of the easiest, and mistakes are rarely attributable to faulty statistical methods. Disappointing results have been obtained most often

either by investigators who have collected larger numbers of observations that were uncritically made, or by those who have not taken the trouble to secure comparable controls. The setting up of adequate controls is probably the chief technical difficulty. Experimentation on such a scale with the illnesses of people is often frowned upon. It is also the common experience that a small number of favorable results leads many of the more optimistic practical physicians to question whether it is ethical to withhold the therapy from enough impartially selected patients to provide adequate controls. The use of statistical data for judging therapeutic efficiency might become infrequent due to such complexities in its use were it not indispensable in certain situations. When the rationale of a measure is not well enough understood to provide objective evidence of cure in a single case, statistics are the only resource. Even where a thoroughly rational method of observation of the effects of therapy is known, additional information of importance such as the general death rate, complication rate and relapse rate, may be determined by means of statistics.

The classification of therapeutic testing methods used above is not exhaustive. It is obvious that the skillful use of such methods depends upon the alteration and adaptation of the technic to suit each individual disease and therapy. The value of this discussion is thought to lie in pointing out the possibility and emphasizing the desirability of careful, conclusive trials of therapeutic measures in man.

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CASE REPORTS

SPONTANEOUS SUBARACHNOID HEMORRHAGES AND THEIR RELATIONS TO RUPTURES OF SMALL ANEURYSMS IN OR NEAR THE CIRCLE OF WILLIS *

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DURING recent years the accurate clinical diagnosis of the nature and localization of intracranial vascular accidents has been greatly advanced, thanks to more careful clinical pathological studies on the one hand, and to the application of the methods of cerebral angiography through the injection of thorotrast or other contrast substances, on the other. In particular, the hemorrhages into the subarachnoid space in the region of the circle of Willis with filling of the cisterna can now be usually recognized with certainty and appropriate treatment can be instituted early. The case reported here illustrates well the symptomatology and the results of prompt treatment in a case of sudden subarachnoid hemorrhage.

CASE REPORT

The patient, Beniditto M., white, 52 years of age, a contractor, was admitted to the Osler Clinic (service of Professor Warfield T. Longcope) on the evening of February 1, 1936, with the complaint of severe headache that had started suddenly four days earlier in the occipital region and had gradually become more generalized and more severe.

Family History. The parents of the patient are both dead, the mother having died at the age of 62. He was one of a family of six, four of whom are living and well, one having died of influenza at the age of 15. The family in general has been healthy except for a tendency to obesity. There has been no history of any disease similar to the patient's in his family.

Past History of Patient. Except for measles in childhood and an attack of pneumonia at the age of 12, the patient has enjoyed excellent health except that for many years he has had a monthly headache lasting 10 or 12 hours, apparently migraine. He denies venereal infection at any time in his life.

His habits with regard to food and drink have been abnormal. It is said that he has taken only one meal a day (in the evening). On rising in the morning he has taken one cup of coffee with two small glasses of whiskey. There has been no mid-day meal. He has been a liberal drinker of wine, consuming six or seven bottles daily in the summer time and often as many as 10 bottles daily in the winter time. In addition, he states that he has taken "as much beer as he could get." He smokes from three to six cigars daily.

He has never been operated upon and has suffered no traumata.

About one year ago his eye-sight began to fail and he was fitted with glasses.

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History of Present Illness. Four days before admission to the hospital, the patient, having felt perfectly well until that time, had spent the afternoon at the movies. After supper, the one meal that he eats each day, he had not felt quite up to the mark. About 8:00 p.m. he went from the hot kitchen upstairs to a cool porch to get some clothing and on returning to the warm room he was suddenly seized with a severe, continuous, throbbing headache, beginning in the posterior part of the head and right temporal region and soon spreading over the whole of the head. He went to bed immediately, felt nauseated and tried to vomit within ten minutes after the onset of the headache. He slept some through the night but next day the headache was worse. He felt feverish, sweated profusely and found it difficult to open his eyes or to see what was going on about him and was unable to eat as food caused nausea. He could, however, retain water in the stomach. On the second day, he took 12 pills that came from a drug-store but without any relief. Indeed, the symptoms not only persisted but became intensified. There was no bowel movement during four days despite numerous doses of salts. He was not unconscious or stuporous at any time and remembers coming to the hospital. There is no history of overexertion, excitement or trauma preceding the attack.

Physical Examination (Dr. Mirick and Dr. Harvey). Temperature 101°. Respiratory rate 28. Pulse rate 56. The blood pressure was 150 systolic, 75 diastolic. The patient was evidently suffering severe pain and was so acutely ill that he was disturbed as little as possible during the examination. There was evident photophobia. The patient was somewhat obese and the skin was moist. The pupils were small and reacted well, both to light and on accommodation. There was no nystagmus and no conjugate deviation of the eyes. Examination of the eye grounds was negative. There was some deflection of the nasal septum to the right. Moderate gingivitis. Slight pharyngitis. The glands at the angle of the jaw were palpable but the glands elsewhere were not enlarged. No enlargement of the thyroid gland. There was marked rigidity of the neck and a definitely positive Kernig sign. The lungs and heart were negative. The radial arteries were palpable but not much thickened. Abdomen and genitalia negative. Deep reflexes everywhere normal. Abdominal and cremaster reflexes present. Babinski negative on both sides. There was some tenderness on pressure over all of the anterior part of the head.

Laboratory Tests. *Blood:* red blood cells 5,330,000; hemoglobin 120; white blood cells 13,860; polymorphonuclear neutrophils 80 per cent; eosinophiles 2 per cent; small mononuclears 18 per cent. *Urine:* Sp. gr. 1.020; trace of albumin; no sugar; a single hyaline cast seen; no white blood cells; no red blood cells. *Cerebrospinal Fluid:* Lumbar puncture done in the accident room before sending the patient up to the ward revealed a cerebrospinal fluid that was under pressure of 230 mm. of water. It was grossly bloody, contained 140,000 red blood cells per cu. mm. and 520 white blood cells of which 80 per cent were polymorphonuclears and 20 per cent small mononuclears. On sedimentation the supernatant fluid was yellowish (xanthochromia).

Course in the Hospital. The patient was kept quiet in bed with orders for liquid diet, with limitation of the fluids to 3,000 c.c. He was given paraldehyde occasionally in 20 c.c. doses.

On the following day, February 2, the blood pressure had fallen to 144 systolic and 80 diastolic but the patient still complained of severe pains in the head. In the afternoon he was given a dose of avertin and the blood pressure afterwards fell to 130 systolic and 60 diastolic. Another lumbar puncture was done; the pressure was 210 mm., Queckenstedt negative. Red cell count in the spinal fluid 130,000. White cell count 600. That evening the patient felt much better though he was still drowsy from the sedatives. The headache had become less severe.

On February 3, another lumbar puncture was done. The fluid was blood tinged. About 8 c.c. were withdrawn. The pressure was 240 mm., Queckenstedt negative.

Red blood cells 21,000. White blood cells 420. The headache continued but was not quite so severe. He was given another dose of avertin.

On February 4, the patient complained of frontal headache. There was no vomiting nor any significant change in respiration, blood pressure or pulse. Cerebrospinal fluid (8 c.c.) removed at 8:00 a.m. showed an initial pressure of 210 mm. The fluid was cloudy and of pinkish color. Red blood cells 14,420; white blood cells 230.

Another lumbar puncture was done at 8:00 p.m. The initial pressure was 220 mm. About 18 c.c. of pinkish, slightly cloudy fluid were removed. Red cell count 12,000.

On February 5, lumbar puncture was done in the early morning. The initial pressure was 190 mm.; 7 c.c. of pale pinkish fluid removed; red blood cells 9,700. During the day the patient improved much symptomatically. The blood pressure was 140 systolic and 90 diastolic. The respiratory rate 20. Pulse rate 68. He received no sedatives during that day except a little codeine. At 9:00 p.m. another lumbar puncture was done. The initial pressure was 190 mm.; 10 c.c. of pale yellowish fluid removed. The red cell count was 13,000 in the fluid.

On February 6, in the afternoon, another lumbar puncture was done. The initial pressure of the fluid was 60 mm.; 8 c.c. of pale yellowish fluid removed. Red cell count 130; white cell count 120.

By February 7, the patient had improved so much that he said he felt himself again. The headache had disappeared, he could open his eyes comfortably, the neck was no longer stiff, and the Kernig sign had disappeared. Cultures from the blood and cerebrospinal fluid remained negative.

Diagnosis. In this case there would seem to be but little difficulty in arriving at the following diagnosis:

1. Spontaneous subarachnoid hemorrhage, probably arising from rupture of a small aneurysm in or near the circle of Willis.
2. Migraine.
3. Obesity.
4. Presbyopia.
5. Faulty habits:
 - (a) Inadequate diet;
 - (b) Potatorium.

In the absence of any history of trauma, of chronic arterial hypertension, and of symptoms suggestive of brain tumor, hemorrhage into the subarachnoid space due (1) to injury of the skull and meninges from an accident, (2) to bleeding in a tumor with escape into the subarachnoid space and (3) to intracerebral apoplexy with passage of blood into the ventricles or subarachnoid space could be easily ruled out so that the diagnosis of so-called spontaneous subarachnoid hemorrhage had to be made. Moreover, the sudden onset, with severe headache, nausea and rigidity of the neck indicative of meningeal irritation were strongly suggestive, and the cerebrospinal fluid on lumbar puncture confirmed the diagnosis.

The fact that the patient suffered from migraine (monthly attacks) is of some interest, since some authors (especially Goldflam) have emphasized the possibility of subarachnoid hemorrhage of vasoneurotic origin, a point that I shall refer to later.

INCIDENCE OF SPONTANEOUS SUBARACHNOID HEMORRHAGE

The frequency of occurrence of so-called spontaneous subarachnoid hemorrhage has only recently begun to be realized. Though the condition was described as long ago as 1886 by Bramwell, it is only in recent years that the symptomatology has been studied carefully enough to permit of the recognition

of a characteristic syndrome that permits of diagnosis during life and the institution of helpful treatment promptly. Even today, many cases, especially those of milder type, are almost certainly overlooked; recovery in such milder cases by natural processes is the rule.

ETIOLOGY AND PATHOGENESIS OF SPONTANEOUS SUBARACHNOID HEMORRHAGE

Hemorrhage into the subarachnoid space due to traumatic laceration of the meninges, to hemorrhage into neoplasms that rupture to the surface, and hemorrhage because of diapedesis in blood dyscrasias are not included under the term spontaneous subarachnoid hemorrhage; in the latter the extravasation of blood into the subarachnoid space is due to spontaneous rupture of a blood vessel. As to the cause of such spontaneous rupture there has, through the years, been much discussion. Formerly, syphilis was thought to be an important cause but this idea has been shown to be erroneous; though in very rare instances syphilis may be the cause of a spontaneous subarachnoid hemorrhage it certainly cannot be a common cause.

In older patients, arteriosclerosis with chronic arterial hypertension has been thought of as the cause and in some cases this explanation has been found to be correct.

Another idea that has been promulgated is that some spontaneous subarachnoid hemorrhages may depend upon vasoneurotic influences. Thus Goldflam has suggested that the hemorrhage may be due to a functional disturbance of vasomotor control similar to what is seen in migraine, Raynaud's disease, and erythromelalgia; after abnormal vasoconstriction active hyperemia takes place and capillary oozing in the subarachnoid space results. Goldflam stated that in five of his 13 cases of subarachnoid hemorrhage the patients suffered from true migraine. It is interesting that the patient reported in the clinic today has also suffered from migraine throughout his life. A study of the bibliography of subarachnoid hemorrhage shows, however, that migraine is relatively rare in association with such hemorrhage and Goldflam's hypothesis seems to me to be untenable.

Though spontaneous subarachnoid hemorrhage may occur at any age, it is most common in young adults and is quite common in children. In recent years the idea that such subarachnoid hemorrhage depends in the main upon a primary weakness of the muscular coat of the arteries has gained ground; the very frequent association of subarachnoid hemorrhage with small aneurysms in the arteries at the base of the brain at the junction of a larger artery with a smaller branch strongly corroborates this view.

As early as 1859, Sir William Gull pointed out that small intracranial aneurysms were much more common than was usually thought and were often overlooked at autopsy since the sac is often small, thin and transparent, and the changes following rupture may easily obscure the little sac. At that time he said that whenever young persons die with symptoms of ingravescent apoplexy and after death a large effusion of blood is found, especially in the meshes of the pia mater, the presence of an aneurysm is probable.

The careful studies of C. P. Symonds (1924) also favored unrecognized aneurysm of congenital origin as the probable cause of obscure cases of subarachnoid hemorrhage.

Thanks to the exhaustive studies of Dr. Wiley D. Forbus, formerly of our department of pathology here, the origin of miliary aneurysms of the superficial

cerebral arteries seems definitely to have been found. In a negro who died at the age of 24 with typical symptoms of spontaneous subarachnoid hemorrhage he found five small saccular aneurysms involving the left middle cerebral and the right and left anterior cerebral arteries and there had been rupture of the aneurysm of the right anterior cerebral artery into the subarachnoid space. After careful gross and microscopic studies he found that the aneurysms arose only from vessels belonging to the carotid system, that they were all located at points of bifurcation of the vessels, that there was a total absence of evidence of acute or chronic inflammation in connection with the aneurysm, that there was a definite defect in the muscular coat at numerous points of division in the right and left middle cerebral arteries, and that the location of aneurysms corresponded exactly to the location of muscular defect in the wall.

Such defects in the muscularis seem to date from embryonic life. They give rise to focal weakness in the vessel wall and may be followed by degeneration of the internal elastic membrane due to continued overstretching of that membrane, after which aneurysm can develop. Though Tuthill has attempted to refute these findings of Forbus, the majority of clinicians and pathologists interested in the subject are inclined to give full credence to the views expressed by this investigator. It is interesting that the most frequent defects in the muscularis in the arteries in the circle of Willis are at the point of junction with some branch or bifurcation, just the point at which the pressure in the blood vessel is maximal.

THE CHARACTERISTIC SYMPTOMATOLOGY OF SPONTANEOUS SUBARACHNOID HEMORRHAGE

When a subarachnoid hemorrhage is not too large or profuse, it is followed by a series of symptoms and signs that are very characteristic and make the diagnosis certain. These may be summarized as follows:

1. A sudden onset, often with a feeling as though something had "snapped" in the head and followed by severe occipital pain which later tends to become generalized.

2. Nausea or vomiting almost immediately after onset.

3. Within a few hours marked rigidity of the muscles of the neck with positive Kernig and Brudzinski signs.

4. On cautious lumbar puncture, blood will be found evenly distributed throughout the fluid in each of three successive tubes.

If these four symptoms and signs are found, the diagnosis is very easy.

When the subarachnoid hemorrhage is greater, mental confusion, agitation or even coma, may quickly follow the onset, and with very large hemorrhages there may be compression of the medulla oblongata with disturbance of respiration, marked bradycardia, and marked rise in blood pressure.

Death sometimes occurs very quickly in large hemorrhages, but if death does not occur the larger hemorrhage will be followed by bradycardia, photophobia, often choking of the optic discs, sometimes nystagmus and anisocoria, and sometimes pyramidal tract symptoms with positive Babinski sign.

Within a few hours after a subarachnoid hemorrhage the temperature begins to rise and slight fever continues for a time accompanied by polymorphonuclear leukocytosis. If later lumbar punctures are carefully done and the red cells are

allowed to sediment, the clear supernatant fluid shows a definite yellow tinge (xanthochromia). The cerebrospinal fluid shows a greater number of white blood corpuscles than would correspond to the amount of blood present, indicating some inflammatory reaction on the part of the meninges. These findings in the cerebrospinal fluid in subarachnoid hemorrhage were so well described by Froin that but little has been added since he made his studies.

Attempts have been made to differentiate between subarachnoid hemorrhage from the anterior group of vessels (internal carotid, middle cerebral and anterior communicating arteries) and hemorrhages occurring in the posterior group (posterior communicating arteries, posterior cerebrals, basilar artery, vertebral artery). In the former, pain in the ophthalmic division of the nervus trigeminus is prone to develop, along with weakness or paralysis of the eye muscles and sometimes with exophthalmos. In hemorrhage from the posterior group, one sometimes sees hemiplegia or paraplegia, dysarthria, dysphasia, or mild cerebellar symptoms, particularly when the basilar artery bleeds.

The small aneurysms that most often give rise to these subarachnoid hemorrhages are rarely large enough to produce symptoms before hemorrhage takes place. If they should be large enough, the symptoms are as a rule neighborhood symptoms due to mechanical pressure.

TREATMENT OF SPONTANEOUS SUBARACHNOID HEMORRHAGE

If the patient is seen within 24 hours after the onset of the first symptoms (severe pain in the head, nausea and vomiting, and stiffness of the neck), the question of lumbar puncture for examination of the cerebrospinal fluid at once arises for it is desirable to decide as early as possible whether a meningitis is present or whether we have to deal with intracranial hemorrhage (either subarachnoid or intracerebral). If there be subarachnoid hemorrhage there is always some danger in making a lumbar puncture during the first 24 hours, but if it be very cautiously done a little fluid sufficient for the making of the differential diagnosis can be withdrawn without danger. If the fluid is bloody in three separate portions we can be sure of subarachnoid hemorrhage. In milder cases one will be satisfied with this for the moment, keeping the patient at rest in bed with the head elevated and administering sedatives for the pain. If the blood pressure be high, the withdrawal of from 300 to 500 c.c. of blood from a vein at the bend of the elbow would be indicated.

In severer cases in which a comatose condition develops quickly after onset or in which there are symptoms of compression of the medulla or pons indicating a larger outflow of blood, it may be necessary either to withdraw more fluid by the lumbar route or, perhaps better, by means of cisternal puncture as a life-saving measure, being cautious, however, not to reduce the pressure to below half the initial figure. In a few cases of severe hemorrhage, surgeons have ligated one internal carotid artery.

After the first 24 hours, cautious lumbar puncture may be done once or twice in the 24 hours with removal of relatively small amounts (3 to 5 c.c.) of fluid, for the relief of the pain in the head and to help in drawing off the blood from the cisternal area. Some are strongly opposed to therapeutic repetition of lumbar punctures, thinking that the value of these punctures has been over-rated and maintaining that Nature does just as well without interference, or even better.

Borok goes so far as to say that lumbar puncture in the treatment of subarachnoid hemorrhage is "absolutely contraindicated"; even for diagnosis he rejects it unless the clinical examination alone will not establish it, in which event he insists upon limiting the amount of cerebrospinal fluid withdrawn to 1 or 2 c.c. In our experience here, though in some cases a single lumbar puncture may suffice, in others repetition of lumbar puncture has been helpful in treatment provided the precautions mentioned have been observed.

After the acute symptoms have passed, the patient should be kept quietly in bed for at least eight weeks to permit of repair of the vessel wall, after which he may be allowed in a chair for an hour the first day, two hours the second day, and three hours the third day; then he may be allowed to walk about a little, avoiding, however, any sudden physical exertion or strong emotion. And since subarachnoid hemorrhage is prone to recur in patients who have had one attack, the mode of life should be carefully regulated ever afterward. The patient's habits should be definitely prescribed, with avoidance of any excess of alcohol or tobacco. Constipation with straining at stool should be guarded against. The prognosis is relatively good, however, and more than 50 per cent of the cases recover if treated in the way mentioned.

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PERIARTERITIS NODOSA *

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As long as the exact status of periarteritis nodosa remains undetermined it will continue to hold the attention of the profession, as it has since the first description approximately 70 years ago. Many cases have been reported in excellent detail, the pathological picture well defined, the experience of the workers abroad and on this continent completely summarized. Bacteriological studies and animal inoculations have not given uniform results. Lately the clinical side has received a major emphasis in the attempt to formulate a picture more easily recognized during life and, perhaps, at an earlier stage of the disease.

Of uncertain etiology, periarteritis nodosa seems to be related to the rheumatic group of diseases, its coexistence with rheumatic endocarditis being noted too frequently to be disregarded.^{1,2,3} Apparently divergent views, that it is due to a filterable virus, that it is a form of hyperergy to some bacterial organism, that it is closely related to rheumatic fever, may not be irreconcilable. Schlesinger and Signy⁴ have lately presented experimental evidence of a virus as a causative agent in acute rheumatism, and Swift, Derick and Hitchcock⁵ have suggested that rheumatic fever itself is a hyperergy to a non-hemolytic streptococcus. In the same patient the distinguishing marks of periarteritis nodosa and of rheumatic fever may both be found; in other instances "the lesions of small vessels in rheumatic fever are so similar microscopically to some of the pictures in periarteritis nodosa that it would be difficult to distinguish the two."⁶

In some instances the gross appearance of the lesions permits of identification and the diagnosis has been made clinically during operation. The presence of nodules and aneurysms along the course of the middle-sized arteries gives a characteristic appearance, the arteries of the mesentery being peculiarly open to inspection. The diagnosis is often, however, made only on microscopic study and it has been established by the routine postoperative examination of specimens of the appendix, gall-bladder, kidney and vas deferens. When the disease is clinically suspected, examination of excised nodules, skin or muscle is often confirmatory, but the absence of the diagnostic lesion in the biopsy does not preclude the existence of the condition in the arteries of the internal organs where the lesions are most often found, particularly in the kidney, mesentery, liver and heart. The arteries involved are the middle-sized ones, those of the size of the coronaries and less, the large arteries and the capillaries escaping. The condition may be localized to a small area or widely distributed but, even in the latter instance, the arterial changes are not continuous along the entire length of the artery but appear at different levels, the lesion beginning and ter-

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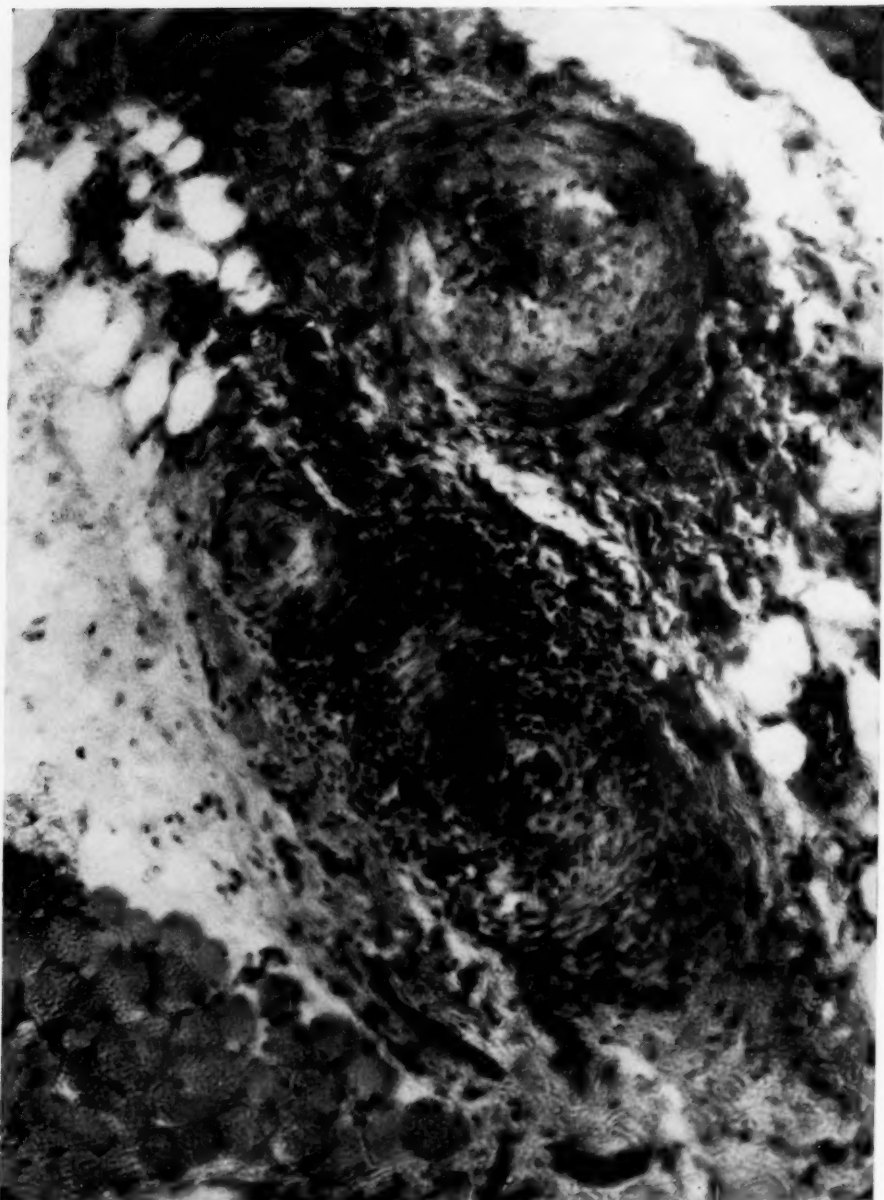


FIG. 1. Advanced perivascular infiltration involving small arterioles and venule. Marked swelling and edema of intima seen in the larger arteriole.

minating quite abruptly. Apparently the toxic agent follows the periarterial lymphatics and attacks the artery at the site of entrance of the vasa vasorum. This distribution is not characteristic of periarteritis nodosa alone, Klotz⁷ having shown a similar situation of lesions in typhoid fever, *Streptococcus viridans* infection, etc. However, the character of the lesion developed in these areas is pathognomonic. The earliest and mildest lesions consist of an exudate in the adventitia—a non-suppurative inflammation. A further degree initiates the

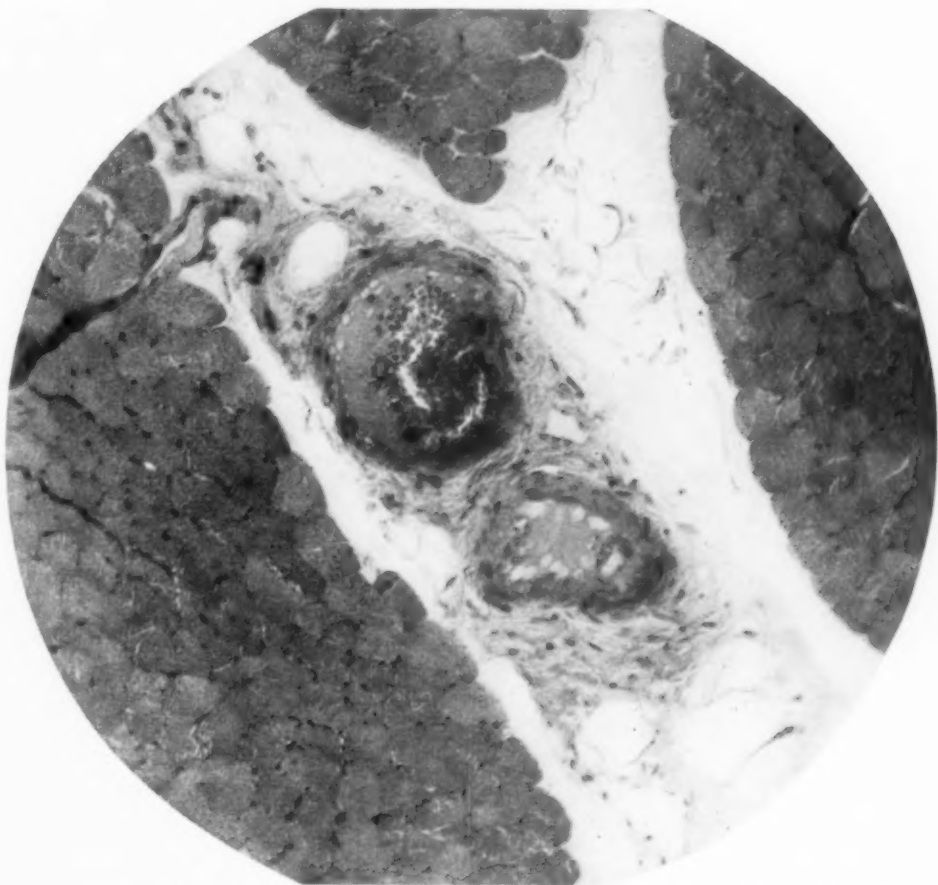


FIG. 2. Hyalinized thrombus filling one small vessel and partially occluding the other.

striking and typical picture, a hyaline degeneration of the media with little or no cellular infiltration. Continuation of the toxic action is followed by fragmentation of the elastica, loosening and exfoliation of the intima, weakening of the entire wall and the formation of aneurysms with thromboses of the hyaline type and canalization of the clot. Repair may take place at any stage so that fibrosis may occur before the formation of aneurysms, in which case the clinically important nodules are not formed; or, the condition may progress to aneurysmal rupture with formation of ecchymoses into the skin or fatal hemor-

rhage into some of the cavities, depending on the particular arterial areas involved. The veins are sometimes affected but do not form aneurysms or nodules.

The disease is rare, Klotz finding no example in over 3,000 autopsies until two patients suffering from the disease were admitted to the hospital on the same day and went to autopsy within four weeks of each other. Lamb⁸ saw two cases within a year, but a review of the sections of all cases of nephritis occurring at the Presbyterian Hospital over a period of six years showed no case of periarteritis nodosa. Bernstein⁹ reports three cases from the Johns Hopkins Hospital and the finding of four other instances of the disease in the review of 13,000 autopsies. It is seen in children and the aged, in both sexes but most often in males in the middle years, in many races.

The recognition of the disease during life has been exceptional. At times the course is acute, of only a few days' duration; or dramatic, presenting only the picture of its surgical complications, intra-abdominal hemorrhage or intestinal obstruction, which overshadow the underlying condition. In these fulminant cases a proper diagnosis is not to be anticipated before operation. But other cases evolve more leisurely and permit a more careful review of the bizarre features. Careful analyses of the reported cases and vivid representation of the clinical pictures by students of the disorder have established criteria that permit the intravital diagnosis, at least in the more fully developed stage. The basic symptoms are chlorotic marasmus, peripheral neuritis, nephritis and gastrointestinal complaints. The progressive weakness and the sense of ill-being are prominent; anemia may or may not be conspicuous. To these symptoms of multi-system disease various other apparently unrelated phenomena are added. A febrile temperature is almost always found, and edema, perhaps fleeting and not necessarily dependent, is frequently noted. Pain in the muscles and joints is usual, the pulse is often accelerated and the blood pressure elevated. Leukocytosis is practically always seen if counts are repeated, and, although eosinophilia is not always present, its occurrence is suggestive. Palpable nodules and ecchymoses may be seen along the course of the arteries, the liver is usually palpable, the spleen sometimes. Many combinations of these findings are sufficiently unusual to suggest biopsy study.

The outcome is almost invariably fatal and no more favorable reports are at hand than of those few who have gone into remission. One of Arkin's cases¹⁰ is particularly illuminating, and, at the same time discouraging, in that the patient recovered from the acute phase of the disease and four years later died from its scars—with a generalized occlusive picture, ischemia of the major organs and function impaired below the vital level. Autopsy showed no acute process of the disease. It is not unlikely that there exists a form milder than the usual fatal one but it is at present below the diagnostic level.

The manner of exitus is dependent upon the course of the disease and the distribution of the lesions. With a slow sclerosing process, the termination may be that of vascular nephritis or of cardiac failure. Most often it is sudden from arterial rupture and hemorrhage, frequently intra-abdominal, perhaps meningeal or pulmonary. The hemorrhage may be beneath the capsule of the liver or the spleen. Mesenteric thrombosis is not rare and bronchopneumonia and pericarditis have been recorded as terminal agents.

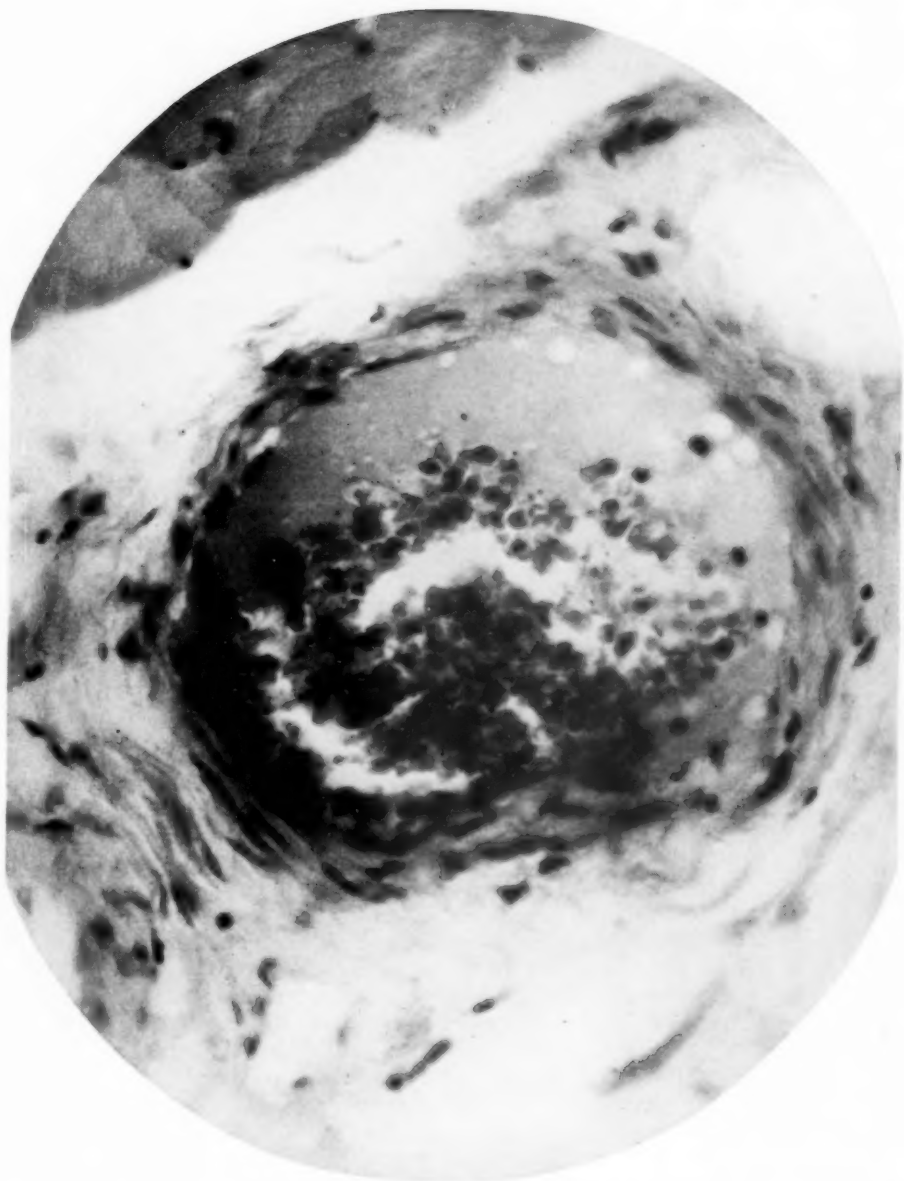


FIG. 3. High power of vessel shown in figure 2, with hyalinized clot, blood cells and pigment cells.

CASE REPORT

R. C. B., an unmarried clerk, 40 years of age, presented himself for examination at the office September 18, 1935, complaining of fever, numbness of the right foot, loss of weight, strength and endurance, and of an indescribable sense of ill-being.

Present Illness: He had not felt well all spring, there had been soreness in the joints and muscles without swelling, he was constipated, and he had suffered from an attack of a perennial type of hayfever. The previous June 10 he had gone to Mississippi on vacation but felt too badly to hunt or fish according to his custom, and, noticing the fever, took quinine for two weeks without relief; he then consulted a physician who prescribed atabrine. The fever was interrupted but soon returned and persisted. He returned to his work but progressively felt weaker and less able to perform his duties efficiently. In August "the cords" above the testicles swelled for one day; on September 7 the right foot went to sleep, the ankle swelled for a few days and felt like a sprain, without injury or discoloration. The swelling soon subsided but the numbness persisted. During the summer he lost 16 pounds in weight, the temperature during this period ranging from 99 to 101° F.

Past History: Raised in Mississippi, he went through measles, mumps and whooping cough. At nine years he was sent to a hospital in New Orleans with "flux." At one time, together with all his classmates who consented, he was given treatment for hookworm but he does not recall a stool examination. There was some history of malaria in childhood and he was in the University of Virginia Hospital for this condition at 18 years of age and took quinine for some time afterwards. At 23 years he acquired a specific urethritis for which he was adequately treated. For 15 years afterwards he was occasionally seen medically for partial impotence and five years ago atrophy of the veru montanum was noted. There was some question as to whether or not strong silver applications had caused the condition. At this time he expressed the opinion to the attending physician that he was becoming senile at an early age. At 22 years he first suffered from a perennial type of hayfever, followed by asthma. At that time he was working in an oil refinery, and exposure to the fumes of sulphuric acid was considered so much a factor that he abandoned his work. Six years ago he was given skin tests for the usual excitants by Dr. A. E. Greer and studied carefully. He reacted to a number moderately and a diagnosis of hypersensitiveness, respiratory, alimentary and cutaneous, was made and a diet constructed. Dr. Greer very kindly supplied the data of this examination and the laboratory and physical examinations were practically negative except as outlined. He remained on the diet for about one year, discarded it then but had no further asthmatic paroxysms. Tonsillectomy was done 8 years ago because of tonsillar infection and 5 years ago he had hemorrhoids of mild degree. He did not have rheumatic, scarlet or typhoid fever. Each winter a week's "flu" was suffered. There was little appetite and, if food were forced, a feeling of pressure and discomfort was experienced. The diet was well balanced. There had been no jaundice, no colic, no hematuria. He thought the stools were at times tarry. Best weight was 148 pounds during the war; when first seen it was 127.5. He took little exercise, but his wind was not good. He was fidgety and easily fatigued. Alcohol, tobacco and coffee were used very moderately.

Family History: The father is still a locomotive engineer at 72; one brother and two sisters are living and well. The mother died at 60 of arteriosclerosis after an illness of only one week in which "brownish spots" were conspicuous.

Physical Examination: A sandy complexioned man of middle age, well educated, alert and not acutely ill in appearance. Height 65¾ inches; weight 127½; temperature 99°, pulse 76.

The pupils reacted to light and distance, the sclerae and conjunctivae were clear, there was no nystagmus, no exophthalmos, no ptosis or ocular palsy. The nares were open, the facial muscles normal, no mastoid tenderness was present and there were

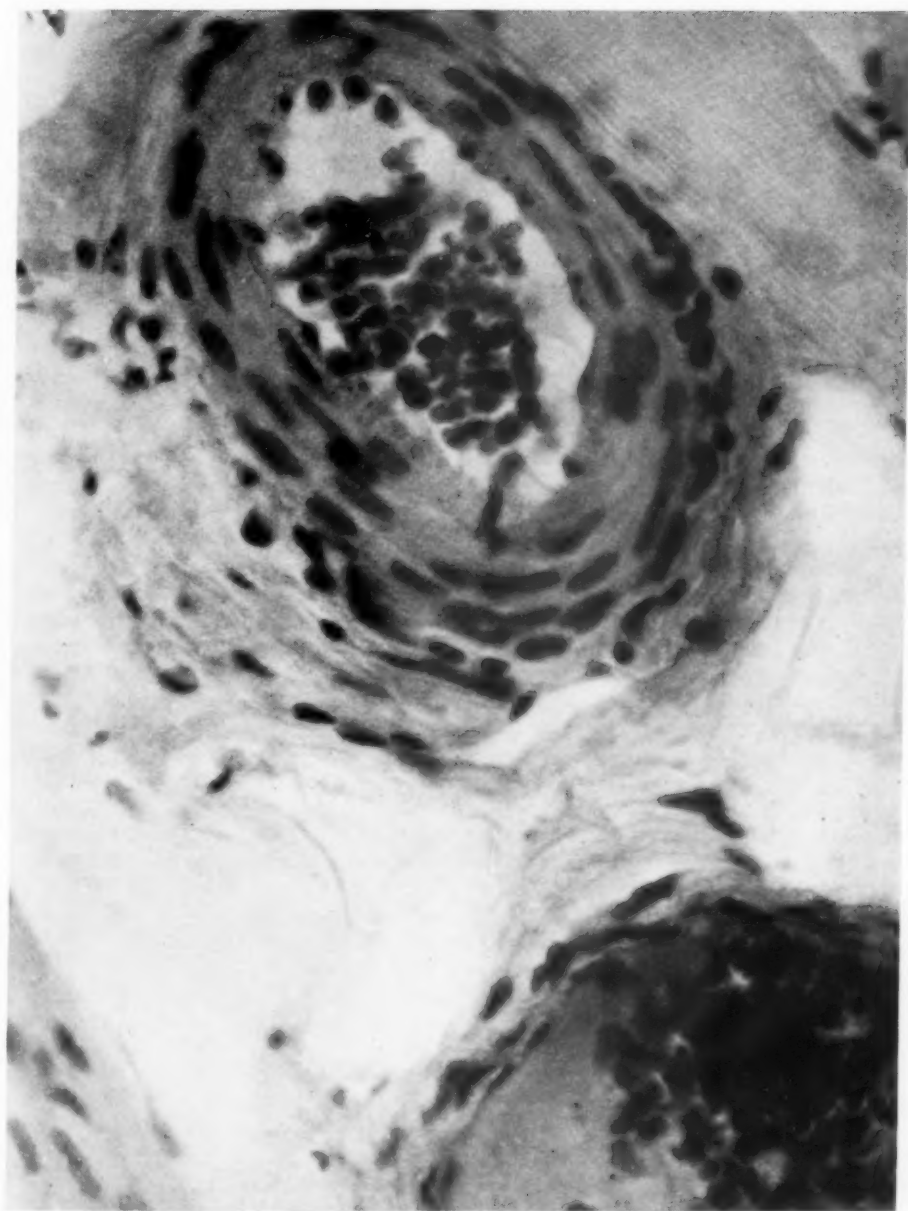


FIG. 4. Arteriole without coagulum showing early swelling of intima and infiltration of the media and adventitia with plasma cells and lymphocytes.

no topi and no discharge from the ear. No sinus tenderness was elicited. The pharynx was negative, the tonsils had been removed with some lymphoid return. Pyorrhea, grade 1, was present; there were no devitalized teeth. The tongue was protruded in the midline without tremor or atrophy. The sinuses transmitted light clearly. The cranial nerves were negative.

There was no adenopathy. The thyroid was just palpable and otherwise negative. The spine was straight, without tenderness.

The chest was well-formed; anteriorly, the upper right lagged; the bases expanded freely; the breath sounds were of lessened intensity and no râles were heard before or after cough. The heart was not enlarged, the left border being 9 cm. from the mid-sternal line. The sounds were of good quality, the rhythm regular, no murmurs were heard. There was no dyspnea, no cyanosis, no abnormal pulsations. The blood pressure on two readings was 140 mm. of mercury systolic and 84 diastolic, and 134 systolic and 84 diastolic.

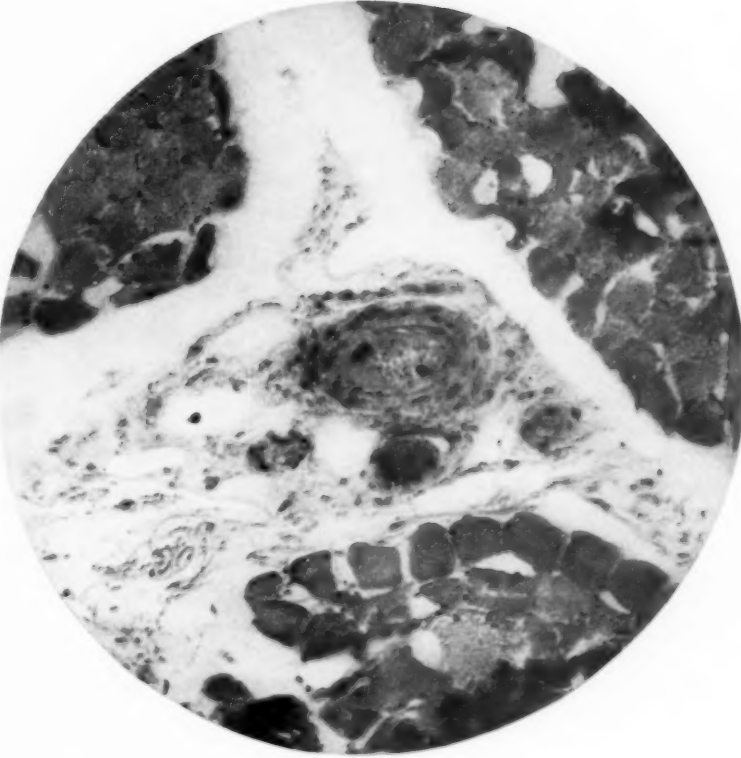
The scaphoid abdomen showed no surgical scars. The right kidney was palpable on deep inspiration but not tender; the spleen came down on inspiration, the tip was easily outlined and tenderness was considerable. The edge of the liver was not felt. The abdominal and cremasteric reflexes were present.

Very slight pretibial edema was noted. There was some atrophy of the calves and tenderness on pressure on these muscles. The patellars were present and normal. Vibration sense was present, as was two-point touch. No Gordon, Oppenheim, Babinski or clonus were found. Temperature and position normal. On the outer side of the right foot, below the external malleolus and extending the length of the foot, an area of hypesthesia was outlined. Likewise there was loss of acute touch sensation on the pads of the toes on the plantar surface, and in the nail region on the dorsal. No foot or wrist drop was present; station, gait and coördination normal. The patient stated that the hands went to sleep but there was no objective sign of neuromuscular disturbance.

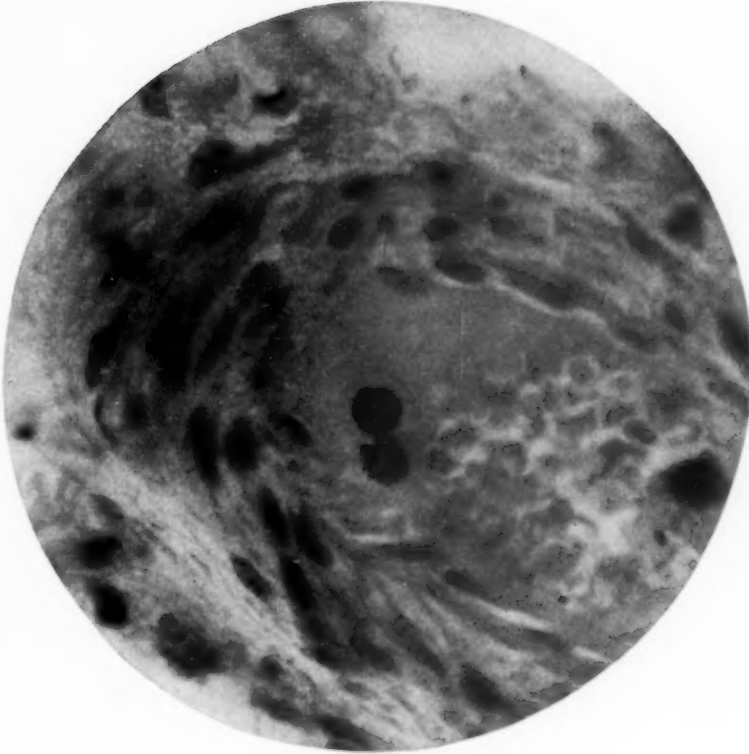
The testes and prostate were atrophied. Nothing abnormal in the epididymis was found. Rectal examination was negative.

A casual specimen of urine was negative except for low gravity. The blood showed hemoglobin 92 per cent, red blood cells 4,580,000, white cells 11,300, with polynuclears 55 per cent, small lymphocytes 29, large lymphocytes 3, large mononuclears 2, eosinophiles 9 and basophiles 2. The Wassermann and Kahn tests were negative.

Summary: This was an unusual picture, one not seen before by the examiner. The patient may or may not have had hookworm disease; he had had malaria in previous years but in the present episode he had failed to obtain expected relief from quinine and atabrine. He had had some of the common infections; he had been found allergic to certain excitants and had had rather unusual relief from asthma. A middle-aged man, with a continuous fever of three months' duration, complaining particularly of marasmus, presented symptoms of multisystem disease: asthma and tendency to dyspnea on exertion; distress after eating a meal of the usual size, and perhaps tarry stools; paresthesias and muscular atrophy; a high normal blood pressure and an increased pulse pressure; a urine of low gravity. In addition there were evanescent swellings of the ankle joint and epididymis, and there was a moderate leukocytosis and a mild eosinophilia. This picture seemed to fit in with the description of periarteritis nodosa, although no nodules had been discovered, there was no anemia and involvement of the gastrointestinal and renal systems was minimal. It was understood that trichinosis might present a similar picture but the chronicity of this case was against that diagnosis. A tentative diagnosis of periarteritis nodosa was made and on September 25 a portion of the right gastrocnemius muscle was removed under local anesthesia by Dr. Herbert Poyner and the specimen given to Dr. Violet Keiller for examination.



A



B

FIG. 5. *A* and *B*. Hyperplastic intimitis; hyaline thrombus with three pigment cells. Two of these are shown in figure 5*B*.
Loss of striation in muscle fibers near lesion.

Laboratory Studies: While the sections were being prepared the following laboratory procedures were followed out: A second blood count showed leukocytes 8,900 with 7 per cent eosinophiles. All slides were negative for malaria. Blood chemistry: Icterus index 6.8; blood sugar 88.0 mg. per cent; non-protein nitrogen 34; creatinine 1.72; uric acid 3.6; chlorides 520. Glucose tolerance: Fasting 88 mg. per cent; one-half hour 130; one hour 149, two hours 200; three hours 154. Phenolsulphone-phthalein: one hour 50, two hours 10. Agglutination against typhoid, para A and B, abortus, proteus $\times 19$, all negative. Stool: pH 7, liquid, brown, trace of bile, no blood, small amount of mucus and detritus, no ova or parasites. Prostatic smear: No pus cells, occasional epithelial cell. Basal metabolic rate: plus 19. Blood culture negative. The electrocardiogram showed a rate of 68 with normal complexes.

Roentgen-ray of chest (Dr. McDeed): Costophrenic angles clear. Evidence is seen of adhesions on the right dome of the diaphragm. Left dome clear cut. There is thickening of the pleura between the right upper and middle lobes. Apical regions relatively clear. No evidence of active tuberculosis or other infectious process.

Ophthalmoscopic examination (Dr. Haden): "The retinal veins of the right eye were somewhat tortuous, the arteries very tortuous. In the neighborhood of the disc the artery light streaks were exaggerated, but further out in the retina they became less distinct and finally disappeared. The arteries were not sharply defined and were bordered by a fuzzy streak, which suggested a disturbance of the lymph spaces. Where the arteries crossed the veins there was a decided depression, as is seen when the arteries have become harder. One minute vessel, a vein, showed three or four minute red swellings along its course. The fundus as a whole presented a fuzzy appearance and its details were not sharply cut. The fundus of the left eye presented similar appearances of the blood vessels to those seen in the right, but not so marked. The appearances of the vessels of either eye were those seen in arterial degeneration of a moderate degree."

When the slides had been studied Dr. Keiller returned a diagnosis of periarteritis nodosa. Because of the known interest in this disease of Drs. Middleton and McCarter of the University of Wisconsin, slides with the history were sent there and an opinion requested. Dr. McCarter wrote under date of Oct. 29, in part, as follows, and his courtesy is hereby gratefully acknowledged: "The biopsy is eminently satisfactory, enough tissue having been taken to allow the pathologist to make a good examination. The larger arterioles show some reaction typical of a rheumatic infection and two small arteries contain typical lesions of periarteritis nodosa. These are fairly acute, and, in view of his present fever, I believe that a poor prognosis is justifiable."

Subsequent Course: The temperature in the last week of September ranged from 98° in the morning to 101° in the evening. On October 18 the blood count showed only 3,700 leukocytes with one eosinophile. In the middle of October he was hospitalized and given artificial fever without notable beneficial result. From October 19 to November 11, the period of hospital stay, except for the periods of therapeutic fever, the temperature was of the saw-tooth, septic type, from 98.6° to 101°, the pulse not following the elevation closely and remaining between 90 and 100. The blood pressure was recorded as 142/80 mm. of mercury, 160/108; it then fell to 138/80 and later rose to 170/90 on November 6. This fall in the blood pressure preceding a second rise has been commented on by Bernstein. The blood counts showed 8,200 to 10,800 leukocytes with eosinophiles 6.5 per cent and 7.5 per cent respectively. The hemoglobin dropped to 76 per cent and the red cells to 3.84 millions on November 6. Further blood cultures and subcultures were negative. The urine continued to be of low specific gravity, 1.017 being the highest and this on only one occasion. Traces of albumin were present.



FIG. 6. Weigert elastic tissue stain. Fragmentation of elastica shown in arteriole. The unstained pigment cells show prominently within lumina of both vessels.

A small scarlet spot appeared on the inner side of the right calf, not nodular, not tender, becoming brown the next day. The spleen was not palpable after the first few days of observation. On dismissal from the hospital he was placed on neo-arsphenamine weekly because of reported benefit from arsenic. On November 23, the blood showed a hemoglobin of 92 per cent, red blood cells 4.78 millions, leukocytes 17,300, polynuclears 85 per cent, small lymphocytes 14, large mononuclears 1 and an absence of eosinophiles. Coincidentally the temperature approached normal and remained there with only an occasional afternoon rise to 100°. The weight loss was eight pounds in three months. A second electrocardiogram was again negative. With the normal temperature there was no subjective improvement. A note on December 15: "It might be hoped from the decline in the temperature that a remission is to be expected. This is probably merely a hope for the patient has not experienced the relief from his symptoms that should accompany a true remission. He states he feels 'as if every cell and fiber of the body were sick.'" No nodules were demonstrated along the course of the arteries; in December there was a questionable one in the right pectoral muscle which was slightly tender. On December 21 he came to the office and stated that he at last thought he could detect definite improvement. He felt better and a persistent, nagging headache had disappeared. Blood pressure was 180 systolic and 100 diastolic; the temperature normal. That afternoon he was found on the floor of his living room in convulsions. These were of a generalized character, and three or four occurred in succession. He did not regain consciousness and died in the ambulance on the way to the hospital. Postmortem examination was refused.

CONCLUSIONS

A case of periarteritis nodosa is reported. This was of such chronicity and extent that a diagnosis during life could be made and confirmed by biopsy.

The striking features were the long period of comparative ill health followed by the onset of persistent fever, peripheral neuritis, muscular atrophy, renal impairment, gastrointestinal symptoms and marasmus.

The use of arsenic brought the temperature to a normal level without relief of symptoms and the disease progressed to its accustomed sudden and fatal termination.

Acknowledgment and thanks are accorded Dr. G. C. Lechenger for the photomicrographs.

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NEISSERIA CATARRHALIS ENDOCARDITIS *

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THAT vegetative endocarditis is due to microorganisms conveyed to the valves through the veins from external foci was first consistently proposed by Emmanuel Winge in a report to the Norwegian Medical Society in 1869. In this country, probably the first demonstration of the infectious nature of acute endocarditis was made before the Chicago Pathological Society by Christian Fenger in 1879. In 1881 Osler showed the New York Pathological Society microscopic preparations from endocardial vegetations containing minute bodies resembling bacteria. However, at this time members of the Society, while accepting the presence of the bacteria, were reluctant to regard them as the cause of the vegetations. They were inclined to believe that the bacteria were merely attendants of the disease, or possibly postmortem invaders, without pathogenic significance. Osler himself seems to have concurred with this view, though four years later his writings show that he fully recognized the infectious nature of the lesion.

Accurate determination of the causative bacteria in endocarditis began approximately at the turn of the century, and in the intervening years many organisms have been incriminated. In acute endocarditis, the principal offenders are well known pathogens, usually the pneumococcus, *Staphylococcus aureus*, gonococcus, or hemolytic streptococcus. Infrequently an organism ordinarily non-pathogenic for man is shown to be the *materia morbi*.

With the exception of the gonococcus and the meningococcus, endocarditis due to Gram-negative diplococci is rare. Examples of the disease caused by *Neisseria pharyngis sicca* have been reported by Schultz,¹ Shaw,² Graef, de la Chapelle, and Vance,³ and Goldstein,⁴ but the following case is, as far as we know, the only recorded instance in this country due to *Neisseria catarrhalis*.

CASE REPORT

History: M. S., a Japanese girl, aged 15, referred by John Wahlen, M.D., of Montebello, California. The patient knew of no definite childhood sickness, but once had been told she had a "leaky heart." The family history was not significant.

About October 30, 1933, she was seized with a chill, followed by fever and headache. She noticed a recurrence of these symptoms several times, and on November 25, a doctor was called who took blood for culture. This culture showed no growth, but the girl did not improve and December 7 she was admitted to the White Memorial Hospital. Her complaints while hospitalized were mainly of frequent pain in the chest and a stubborn cough with little sputum. Several times she complained of severe pain in the right upper abdominal quadrant, for which no cause could be ascertained.

Physical Examination: The physical examination revealed a slightly pale, fairly well-nourished Japanese girl. On numerous occasions coarse râles were noted in the right lung base, posteriorly. The breath sounds were diminished in the left base; those heard over the upper lobes of both lungs seemed normal.

The heart was enlarged to percussion. The rhythm was regular. A loud systolic murmur was heard best over the pulmonary area, where there was also a palpable thrill.

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From the Departments of Medicine, College of Medical Evangelists and the Los Angeles County Hospital.

The abdomen was tender on pressure, particularly in the right upper quadrant. The uterus and adnexa seemed normal. Neurologic examination was negative.

The white blood cell count on admission was 31,250 per cu. mm. with 92 per cent polymorphonuclear neutrophils. The red blood cells numbered 3,600,000 per cu. mm. with 60 per cent hemoglobin. Urinalysis was essentially negative. Roentgen-ray of the chest showed evidence of partial consolidation in the right lower lung field. The blood Wassermann was negative. Repeated blood specimens were taken and a Gram-negative diplococcus was recovered in pure culture.

Course in Hospital: Her temperature curve was septic in type, ranging from 97° F. to 105° F. She became progressively weaker and toward the end somewhat delirious. She died January 12, 1934.

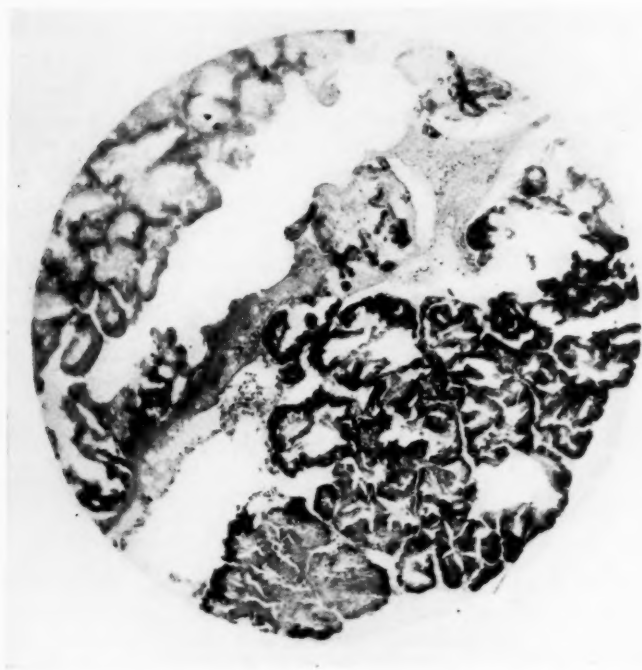


FIG. 1. Section through vegetation from pulmonary valve showing bacterial colonies. (× 60.)

Autopsy: O. B. Pratt, M.D. performed the autopsy in an undertaking parlor where there were no facilities for weighing the organs.

The body was that of an emaciated Japanese girl. No petechiae, edema, or scars were noted.

The pleural cavities contained no fluid. Over the pleural surface of both lower lobes there were patches of fibrinous exudate. The upper lobes of both lungs were crepitant and the cut surfaces dry. Both lower lobes were heavy, dark red in color, and bloody fluid exuded from the cut surfaces. In the right lung two infarcts were found, roughly pyramidal in shape, each measuring about 3 cm. in greatest length. On pressure over the lungs, purulent fluid exuded from the cut ends of the branches of the pulmonary artery.

The pericardium was smooth and glistening. The heart was only slightly larger than normal. The tricuspid valve measured 10 cm. in circumference, and near the

margin of one of its leaflets there was a raised pink nodule 3 mm. in diameter with a rough surface. A large, light brown, friable vegetation filled the conus arteriosus and extended 2 cm. beyond the pulmonary valve into the pulmonary artery. Between the vegetation and the valve ring were two small passages, through which blood had apparently been transmitted. The cusps of the pulmonary valve were not deformed. There was slight ulceration at the site of the attachment of the vegetation, which was separated rather easily from the valve and the heart wall. The mitral ring measured 8 cm. in circumference, and on one of the valve leaflets a nodular vegetation, 4 mm. in diameter, was found at the line of closure. This was broken off in handling, leaving an ulcerated surface. The aortic valve appeared normal.

The liver was somewhat larger than normal and the cut surface was reddish brown. The spleen was about four times normal size. Its pulp was extremely soft and was dark red in color.

No other gross changes of significance were observed.

MICROSCOPIC EXAMINATION

Vegetation of the Pulmonary Valve: Sections showed amorphous eosin staining material containing scattered leukocytes. At the free surface were fibrin and many leukocytes. Colonies of bacteria, apparently micrococci, staining lightly with hematoxylin, were seen near the surface as well as deep in the vegetation.

Tricuspid Valve: Sections showed an ulcerated surface. The base of the ulcer was heavily infiltrated with leukocytes, and there were a number of bacterial colonies resembling those seen in the pulmonary valve vegetations.

Lung: Surrounding an area of infarction, the alveoli were filled with eosin-staining fluid, containing some fibrin. Other alveoli were filled with blood and some were packed with leukocytes. A few colonies of bacteria were seen, each in close relation to a blood vessel. Some arteries were thrombosed and bacterial colonies were seen in the thrombi.

Liver: There was evidence of marked chronic passive congestion and some fatty degeneration.

Spleen: The findings resembled those of acute splenic tumor.

Kidney: Some adhesions were noted in Bowman's capsule and there was an apparent increase of endothelial cells of the glomerulus. The tubular epithelium showed cloudy swelling. Some areas of interstitial tissue were infiltrated with small round cells and leukocytes.

BACTERIOLOGICAL STUDIES

All blood samples taken hourly for 24 hours on December 8 yielded pure cultures of a Gram-negative diplococcus. The number of organisms obtained varied from 1 to 3 per c.c. of blood. An identical strain of organisms was recovered in pure culture at autopsy from purulent material in the thrombosed pulmonary arteries.

On solid medium the colonies were small, rounded, firm, adherent, opaque, colorless, and at first smooth. Older colonies tended to have irregular margins and wrinkled surfaces. Subcultures were made on glucose, meat infusion agar, blood agar, plain agar, Loeffler's blood serum, and dextrose brain broth, on all of which the organism grew readily at 37.5° C. and at room temperature. No gas or acid formed in dextrose, inulin, or mannite. No pigment formed on any medium used. Except in medium containing brain, the cultures soon died, even when frequent subcultures were made. The conclusion was that the organism was *Neisseria catarrhalis*.

Accordingly the cause of death was given as acute bacterial endocarditis due to *Neisseria catarrhalis*.

COMMENT

In 1932, Curtis⁵ reported the case of a physician who, following tonsillectomy, developed acute polyarthrititis. *Neisseria catarrhalis* was recovered from cultures of this man's blood and a diagnosis was made of "acute polyarthrititis, acute endocarditis, and bacteremia of *Micrococcus catarrhalis* origin." The record of this patient's illness closely resembles that of a Mr. L. G., a white male, 21 years of age, who was admitted to the Los Angeles County Hospital, February 7, 1935, complaining of precordial pain and recurrent bouts of chills and fever. For weeks his temperature ranged from 97° F. to 105.5° F., and of 11 blood cultures, eight were positive for *Neisseria catarrhalis*. A soft systolic murmur was heard at the apex, petechiae were seen on chest and abdomen, and the clinical diagnosis was acute endocarditis due to *Neisseria catarrhalis*. In contrast to Curtis' patient, who received sodium iodide, neosalvarsan, salicylates, and cinchophenic acid, this patient was given graduated doses of a *Neisseria catarrhalis* vaccine, prepared from his own blood cultures by Dr. Fisk, Bacteriologist at the Los Angeles County Hospital. From April 27 to May 10 this patient remained afebrile and, feeling much better, he insisted on leaving for his home in Texas. A letter from the local social worker, dated July 4, 1935, stated that he was doing light work.

Since both these patients recovered, the diagnosis of endocarditis was not established and we believe the case reported with autopsy in this communication is the first pathologically proved example of *Neisseria catarrhalis* endocarditis in this country.

In Europe a similar autopsied case of endocarditis due to this organism has been observed and described by Endres.⁶ His patient was a farm worker, 47 years of age, with a definite history of rheumatic fever, followed by heart damage. At autopsy there was evidence of rheumatic involvement of the mitral and aortic valves. (Incidentally, our patient, while giving a history of a "leaky valve," proved to have no pathological evidence of rheumatic heart disease.) Small Gram-negative diplococci were seen histologically in a vegetation on the aortic leaf of the mitral valve. Similar organisms had been recovered from blood cultures and proved bacteriologically to be *Neisseria catarrhalis*. In this case there was a classical embolic glomerulonephritis. In our patient, since the vegetations occurred on the pulmonary and tricuspid valves, embolic phenomena were seen only in the lungs.

While *Neisseria catarrhalis* is found commonly in the upper respiratory passages, and usually possesses little virulence, under favorable circumstances it apparently may become pathogenic. For example, it has been recorded as the etiological factor in meningitis,⁷ pneumonia,⁸ and septicemia.⁹

SUMMARY

A case of fatal endocarditis due to *Neisseria catarrhalis* is reported. *Neisseria catarrhalis* is rarely pathogenic, and as the cause of vegetative endocarditis it must be extremely rare, for we are unable to find another example, with autopsy, in the literature of this country.

A résumé is given of a case of septicemia of *Neisseria catarrhalis* origin. This patient was thought clinically to have endocarditis, but he made a surprising and apparently complete recovery.

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EDITORIAL

BIOLOGICAL FACTORS IN MALARIAL CONTROL

The recent sharp rise in the death rate from malaria in the United States¹ serves as a sharp reminder that the problem of malarial control in this country is not yet solved. To many of us, at least those of us who do not live in a malarial district, it is somewhat surprising to read that over 4,500 died from malaria in this country in 1934, and that the morbidity rate for that year was probably over 5,000,000 cases. Superficially the problem seems a simple one—exterminate the mosquito. Past experience indicates that any effective method of control does indeed depend on destroying the mosquito larvae or eradicating their breeding places. To accomplish this, however, we must know what species to attack, where to find it, and what weapons can be used effectively against it. Some of the complexities of this problem have been pointed out in an interesting way by Hackett.²

Human malaria is transmitted exclusively by certain species of mosquitoes belonging to the genus *Anopheles*. It has been proved that about 40 (out of over 100) species may become infected with malaria and can transmit the disease to man under experimental conditions. Epidemiological studies have shown, however, that under natural conditions most of these species rarely convey malaria, and that 12 or 15 species are responsible for nearly all the malaria of the world. In a given locality, as a rule, only one or at most two or three species are of practical importance. The reasons for the failure of potential vectors of malaria to convey the disease under natural conditions are various. They can be determined only by a minute study of the habits of each species and its relation to its environment in each different region.

In some cases this depends upon the preference of the mosquito for animal rather than for human blood. In the eastern United States, for example, three potential vectors of malaria are abundant. Two of these (*A. crucians* and *A. punctipennis*) are relatively "wild" species, rarely enter houses, and by preference bite animals rather than man. *A. quadrimaculatus*, on the other hand, often enters houses, bites man and animals indifferently and is responsible for nearly all the malaria in this region. The biting habits of the same species may differ in different localities. In the case of *A. maculipennis*, the principal vector in Europe, there are several races whose habits differ in this respect. The race in the coastal districts of Holland, which breeds in brackish pools, bites both man and animals indifferently, and malaria is endemic in these regions. A few miles inland there

¹ As shown by the collected statistics of the U. S. Public Health Service and emphasized at the Symposium on Malaria of the National Malaria Committee and the Southern Medical Association: South. Med. Jr., 1935, xxviii, 736.

² HACKETT, L. W.: Biological factors in malarial control, Am. Jr. Trop. Med., 1936, xvi, 341-352.

is a different race (distinguishable only by the barred markings on its eggs) which breeds in fresh water and prefers animal blood. Here malaria is sporadic. In more primitive districts in which few animals are raised (as in central Russia) this race is driven to bite man and becomes a dangerous vector. For other reasons which are entirely unknown the same species (e.g. *A. subpictus*) may convey malaria in one region (in the East Indies) and not in another (in India), although it is abundant and bites man freely in both.

The character of the breeding places is even more important. *A. quadrimaculatus* in the United States breeds in quiet fresh water in pools or puddles, and where adequate drainage of such areas is possible, the pest can be eliminated to a large extent. This should be practicable for the larger communities, at least, since these mosquitoes rarely travel more than a mile from their breeding places. In Italy, on the contrary, the prevailing species breeds equally well in quiet or flowing water, and drainage does not affect it. In certain districts of Malaya in which the vector (*A. maculatus*) breeds in open flowing streams, by damming the streams and producing a series of pools it has been possible to eliminate this variety and replace it with harmless species. On the other hand in regions like Albania in which there are two vectors which differ in their choice of breeding places, the elimination of one, when a drought dries up the pools, is accompanied by an excessive breeding of the other in the shallow streams. The breeding habits of the same species may differ in different regions. Thus in Java *A. ludlowi* breeds only in salt water, and its depredations are confined to the coastal regions, while in Sumatra it breeds in fresh water and infests much of the island.

A radical change in the environmental conditions in a district may convert a potential vector, previously harmless, into a dangerous transmitter. This occurred when the cultivation of rice was introduced into Sumatra during the war. An epidemic of malaria broke out promptly, due to *A. hyrcanus*.³ This possibility had been excluded, it was supposed, by the fact that this species breeds abundantly in the rice fields of Java and other neighboring islands and there it is not a transmitter.

In the United States the problem seems relatively simple. There is only a single important transmitter, and its breeding places can be eradicated without undue difficulty. The immediate obstacle is the prohibitive cost of carrying out such procedures on an adequately large scale. It is to be hoped that further study will reveal less costly methods of control. Unless it does, we may expect that malaria will continue, at least until the economic value of the peasant exceeds the cost of the public health measures necessary to protect him.

P. C.

³ SWELLENGREBEL, N. H.: Le médecin et l'entomologie, Riv. di Malariol., Sez. ii, 1934, xiv, Supp. to No. 3, 73.

REVIEWS

American Martyrs to Science Through the Roentgen-Rays. By PERCY BROWN, M.D., F.A.C.P., F.A.C.R. 276 pages; 15.5 × 23.5 cm. Charles C. Thomas, Baltimore. 1936. Price, \$3.50.

This small volume presents a brief sketch of the lives of an heroic group of Americans connected with the early history of the roentgen-rays. It is written in a readable style and brings to life those earnest, faithful scientists who, by every sacrifice, including that of life itself, made the advance of roentgenology possible.

Forty years ago this new science was conceived and it has been largely due to the valiant efforts of this illustrious group of men that roentgenology has advanced so rapidly to its present status. It is interesting to note the different channels by which these men entered the field, and their complete absorption in their work, even when suffering the most excruciating pain. Very few of the early pioneers were provided with any protection against the direct effect of the rays. Sometimes the face and chest, and more often the hands, were repeatedly exposed in order to make a satisfactory examination of the patient, or to exploit the "x-rays" in popular exhibitions.

The serious nature of their work so thoroughly dominated their thoughts that they had little consideration for their personal safety. These pioneers lived and died in relative obscurity. They gave their lives to the cause of science, and if ever the term Martyr should be applied, it belongs to them.

The author has inserted a simple glossary for the layman "to clarify the meaning of certain scientific terms impossible to avoid."

The author speaks with authority and modestly refrains from any personal allusions. Anyone interested in the progress of medicine will find this book both interesting and instructive.

H. J. W.

The Pathology of Internal Diseases. By WILLIAM BOYD, M.D., M.R.C.P., F.R.C.P. Second Edition. 904 pages; 16 × 24 cm. Lea and Febiger, Philadelphia. 1935. Price, \$10.00.

In the second edition of this work the author has added many new sections, and major alterations have been made in other sections. The illustrations are excellent. References, especially to the more recent literature, follow each chapter. The author not only describes the morbid anatomy of internal diseases, but also links it to the clinical symptomatology presented by such diseases. At times he perhaps is more positive in his statements than would seem justified by the evidence at hand, and at times the clinical discussion leaves something to be desired. However, one hesitates to criticize what the reviewer considers so valuable a work. The style is forthright and the book throughout maintains its interest. It is highly recommended to students and to practitioners.

W. S. L., Jr.

Common Contagious Diseases. By PHILIP MOEN STIMSON, A.B., M.D. 437 pages; 14 × 20 cm. Lea and Febiger, Philadelphia. 1936. Price, \$4.00.

The clear presentation of the subject matter contained within this manual is striking, for despite its conciseness, the author has avoided disjointed sequences and the impression of incompleteness that a reader is so often left with after reading abbreviated books. There is instead a personal feeling instilled so that the reader may easily imagine himself in the presence of the author.

The introductory chapter on "Infection and Immunity" is discussed mostly from its clinical relationship. The author deals understandingly with these topics, without becoming mired in hypothetical conjectures.

Diphtheria, Vincent's angina, scarlet fever, measles, rubella, pertussis, mumps, chicken-pox, small-pox, meningococcus meningitis and poliomyelitis are the diseases discussed as contagious. All aspects of these conditions are dealt with in an adequate manner. The newer work on the subjects is included and a practical critical evaluation offered. Adequate space is devoted to the various sera being used in both prophylaxis and treatment. Personal experiences are nicely blended in the discussion to confirm or throw doubt upon a conjecture. An adequate bibliography is included at the end of each chapter. A final chapter on the "General Management of Contagious Diseases" is included. And here, especially in the discussion of the management of "Contagion in the Home," is the practical attitude made most apparent.

Photographs and various charts are embodied in the text. Unfortunately the photographs of the exanthems are not colored, hence their value is relatively negligible.

The book is unreservedly recommended by the reviewer for the use of the medical student and practitioner.

J. E. B.

The Human Foot. By DUDLEY J. MORTON. 244 pages; 16 × 23.5 cm. Columbia University Press, New York. 1935. Price, \$3.00.

This book is a most complete treatise on the foot and to a practicing orthopedist is most timely. If it should be read by a sufficient member of medical practitioners, shoe manufacturers, and chiropodists its value would be inestimable.

The book is divided into three parts, covering the evolution, the physiology, and the functional disorders of the human foot. Each part treats thoroughly the various elements of its topic by means of several or more chapters. The text is easy to read, is as free from technical language as is possible, and yet is thoroughly clear and easy to understand.

Part 1 is quite interesting and explains what may lie back of many functional foot disorders. Ordinarily, we rarely realize that the foot of today is expected to do many things for which it originally was not made and this particularly with the handicap of the modern shoe.

Part 2 analyzes thoroughly the varied and complicated activities of the foot in standing, walking, etc. Emphasis is laid upon the well known fact that a normal foot does not need "artificial aid in its function of stance and locomotion." People who have never worn shoes do not as a rule have the foot troubles we hear so much about. This chapter bears analysis and study and will well repay a careful reading. Active exercise is essential to foot comfort and efficiency.

Part 3 considers the possible effects of abnormal development and function, describes the clinical signs and symptoms of each type of disability, and lastly gives good suggestions as to treatment. Emphasis is laid upon the improper use of an arch support, especially of the rigid type. Redevelopment of the weakened structures is the theme of this section and this should be the basis of sound practice. Artificial aids should be used only as auxiliary measures until proof exists that the foot will not respond and must be "crutched" permanently.

All in all the book should be referred to frequently and should find a place in everyone's reference library.

A. V.

The Kidney in Health and Disease. Edited by HILDUNG BERGLUND, M.D., and GRACE MEDES, Ph.D. with the collaboration of G. CARL HUBER, M.D., WARFIELD T. LONGCOPE, M.D., and ALFRED N. RICHARDS, Ph.D., M.D. 754 pages; 16 × 24 cm. Lea and Febiger, Philadelphia. 1935. Price, \$10.00.

This volume is the outgrowth of a symposium in 1930 on the structure and function of the kidney in health and disease. The project was initiated by Dr. Hildung Berglund, then Professor of Medicine in the University of Minnesota. The contributions made at that time have been revised and brought to date by the participants in the symposium. There are 44 contributors and listed among them are many of the prominent investigators of questions pertaining to the kidneys. The book is divided into six parts and 41 chapters. The main divisions are concerned with the anatomy and physiology of the kidney, clinical aspects of renal functions, Bright's disease and other pathologic renal conditions, albuminuria and edema, ocular changes in Bright's disease, and clinical aspects of Bright's disease.

This volume affords an excellent example of what may be accomplished by welding together contributions by many outstanding investigators. It is an authoritative reference work. Each contribution is accompanied by a thorough bibliography. This is a volume which no one interested in kidney problems will wish to be without and any practitioner could read it with pleasure and profit.

W. S. L., JR.

The Crippled and the Disabled. By HENRY H. KESSLER, M.D. 337 pages; 16 × 23.5 cm. Columbia University Press, New York. 1935. Price, \$4.00.

Any study of the problem of the crippled and disabled is necessarily extensive and difficult due to the many types and combinations, both as to areas and senses involved, and to the age periods and variable reactions of each. Dr. Kessler has very thoroughly reviewed the extensive available literature and has analyzed the facts presented from an unbiased standpoint. His suggestions for the correction of the situations as now found are sensible and sound.

The book is divided into seven parts, an appendix and a large bibliography. The disabled are considered generally in Part 1, where the problem as a whole is analyzed with appropriate comments as to the need for a change in the attitude of the disabled toward the community and vice versa.

Part 2 deals with the child problem both here and abroad. Much more definite progress has been made for children than for adults due to the appeal possessed by children and to the activities of fraternal and social organizations. Industrial advancement and the experiences of the War have led to a greater activity in providing care for disabled adults.

Parts 3 and 4 consider the industrially disabled and those injured in war. The care of these two groups has stimulated the development of improved physical and occupational therapy. Statistical tables and many references show the changing situations of these types. An appeal is made for a more universal consideration of the disabled by industry so that a trained cripple may obtain reemployment more easily.

The chronically disabled are considered in Part 5. Special emphasis is laid upon how their needs are and should be met.

The blind, deaf, and deaf-mutes are considered very briefly in Part 6, and the whole picture is summarized in Part 7.

An appendix gives a short summary of the various types of legislation in each State; at the end is a very complete and extensive bibliography which will be most useful to anyone who is interested in the problem of the disabled.

The book is an important addition to a reference library and is very appropriate at the present time.

A. V.

COLLEGE NEWS NOTES

ADDITION TO THE LIFE MEMBERSHIP ROSTER

Dr. Orville H. Brown (Fellow), Phoenix, Ariz., became a Life Member of the College on June 10, 1936.

GIFTS TO THE COLLEGE LIBRARY

Acknowledgment is made of the receipt of the following gifts to the College Library of publications by members:

Dr. J. N. Hall (Fellow), Denver, Colo.—4 books, Volumes I and II, "Borderline Diseases," and Volumes I and II, "Textbook of Legal Medicine and Toxicology";

Major James S. Simmons (Fellow), M. C., U. S. Army—1 book, "Laboratory Methods of the United States Army" (Fourth Edition);

Dr. Charles F. Morsman (Fellow), Hot Springs, S. D.—2 reprints;

Dr. Glenn D. Carlson (Associate), Dallas, Tex.—1 reprint;

Dr. John P. Hilton (Associate), Denver, Colo.—1 reprint.

MEETING OF THE NEW JERSEY MEMBERS

Under the Governorship of Dr. Clarence L. Andrews, Fellows and Associates of the College from New Jersey held a luncheon-meeting at the Claridge Hotel at Atlantic City on June 3. Dr. Andrews acted as Chairman and Toastmaster. Dr. Ernest B. Bradley, President of the College, Lexington, Ky., Dr. O. H. Perry Pepper, First Vice-President, Philadelphia, Pa., Dr. William D. Stroud, Treasurer, Philadelphia, and Mr. E. R. Loveland, Executive Secretary, made short addresses concerning various College activities. Other guests present included Dr. E. J. G. Beardsley, of Philadelphia, Governor for eastern Pennsylvania, and Dr. Lewis B. Flinn, of Wilmington, Governor for Delaware. Twenty-five Fellows and ten Associates from New Jersey were present.

Dr. George R. Minot (Fellow), Boston, Mass., and Dr. Hugh J. Morgan (Fellow), Nashville, Tenn., were elected Vice-President and Secretary, respectively, of the Association of American Physicians at its annual meeting in Atlantic City, May 6.

Dr. W. A. Dearman (Fellow) has removed from Gulfport, Miss., to Whitfield, Miss., where he has assumed the duties of Assistant Superintendent of the Mississippi State Hospital.

Dr. Ralph Pemberton (Fellow), Philadelphia, addressed the Lehigh County (Pa.) Medical Society at Allentown, April 14, upon Arthritis; he gave a Seminar at the Robert Packer Hospital, Sayre, Pa., May 27, on Arthritis; and he addressed the Medical Society of the County of Saratoga, New York, June 4, upon the same subject.

Dr. Joseph Hajek (Fellow), New York, N. Y., has been elected Secretary of the Section of Medicine of the New York Academy of Medicine.

Dr. Hyman I. Goldstein (Associate), Camden, N. J., presented a paper on "Antispasmodic Therapy in Gastro-Intestinal and Biliary Tract Diseases" at the 170th annual meeting of the New Jersey State Medical Society, Section on Gastro-Enterology, at Atlantic City, June 4. His paper was discussed by Dr. Samuel Weiss (Fellow), New York, and by Professor Charles M. Gruber, of Philadelphia.

Dr. Goldstein also discussed constipation at the convention of the National Society for the Advancement of Gastro-Enterology at Atlantic City, June 5.

At the annual meeting of the Arkansas Medical Society at Hot Springs National Park, Dr. George B. Fletcher (Fellow), Hot Springs National Park, was installed as President. Dr. Arthur G. Sullivan (Fellow), Hot Springs National Park, was elected a Vice-President and Dr. William R. Brooksher (Fellow), Fort Smith, as Secretary.

Dr. Leon Unger (Associate), Chicago, addressed the Chicago Society of Allergy, May 18, on "Asthma in Children; Results of Treatment."

Dr. William H. Marshall (Fellow), Flint, Mich., has been elected President of the Northern Tri-State Medical Association.

Dr. James H. Donnelly (Fellow), Buffalo, is President of the Buffalo Academy of Medicine.

Dr. Walter W. Palmer (Fellow), Dr. Alvan L. Barach (Fellow), both of New York City, were lecturers on the program of the ninth annual postgraduate day of the Mahoning County (Ohio) Medical Society at Youngstown, April 30.

Dr. Edgar A. Hines (Fellow), Seneca, S. C., has been reelected Secretary of the South Carolina Medical Association. Dr. Hines has served as Secretary for 26 years.

Dr. Howard T. Karsner (Fellow), Cleveland, Ohio, has been elected Secretary of the American Association of Pathologists and Bacteriologists at their annual meeting in Boston during April.

Dr. Jesse D. Hamer (Associate), Phoenix, Ariz., was installed as President of the Arizona State Medical Association at its annual meeting recently.

Dr. Charles Wolferth (Fellow), Philadelphia, delivered a lecture on "Observations on the Mechanism and Clinical Interpretation of Heart Sounds" in connection with the annual postgraduate course of the Indiana State Medical Association at Indianapolis during April.

Dr. George P. Pratt (Fellow), Omaha, Nebr., presented a lecture on coronary disease at the regular meeting of the Southwestern Iowa Postgraduate Medical Society in the spring.

Dr. Soma Weiss (Fellow), Associate Professor of Medicine at Harvard Medical School, was one of the speakers on a cancer symposium conducted in connection with the 84th annual session of the Maine Medical Association in Rangeley, June 21 to 23.

Harvard Medical School will observe its Tercentenary, September 14 to 15. The Harvard Medical Alumni Association will hold its annual meeting and dinner in Vanderbilt Hall on the evening of September 15, the dinner having been postponed from its usual time in June to encourage participation of as many graduates as possible in the Tercentenary celebration. Dr. George R. Minot (Fellow) will act as Chairman of a symposium on nutrition and the deficiency diseases; Dr. James H. Means (Fellow) will act as Chairman of a symposium on the endocrine glands.

The Medical Society of New Jersey held its 170th annual meeting at Atlantic City, June 2 to 4, under the Presidency of Dr. Marcus W. Newcomb (Fellow), Browns Mills. Among guest speakers were Dr. Israel M. Rabinowitch (Fellow), Montreal, "Medical Complications in Diabetes Mellitus," and Dr. Arthur C. Christie (Fellow), Washington, D. C., "Medical Progress Under the Leadership of the Medical Profession."

Dr. Ross McC. Chapman (Fellow), Towson, Md., was elected President-Elect of the American Psychiatric Association at its annual meeting in St. Louis, May 4 to 8.

Sir Frederick G. Banting (Fellow), Toronto, and Dr. Joseph B. Collip (Fellow), Montreal, addressed the annual meeting of the Canadian Medical Association at Victoria, B. S., June 22 to 26, on "Silicosis Research" and "Significance of Recent Investigations of the Ductless Glands," respectively.

Dr. F. M. Pottenger (Fellow), Monrovia, Calif., presented the Phi Rho Sigma Lecture at the University of Colorado School of Medicine, Denver, May 7, on "Physiological Approach to the Diagnosis and Treatment of Tuberculosis."

The Academy of Medicine of Washington was organized April 28, with Dr. William A. White (Fellow), President, Dr. Earl B. McKinley (Fellow) and Dr. Matthew W. Perry (Fellow) as Directors. The membership will be limited to 60 resident members and 30 associates or non-resident members. Membership is open to non-medical as well as medical men, since no special distinction has been made between the medical sciences and allied sciences.

Dr. Guy C. Jarratt (Associate), Vicksburg, Miss., has been elected one of the Vice-Presidents of the Mississippi State Medical Association.

Dr. Edward Rose (Fellow), Philadelphia, addressed the Gloucester County (N. J.) Medical Society recently on "Basal Metabolism and Its Relation to Disease."

Dr. Louis E. Viko (Fellow), Salt Lake City, is President-Elect of the Utah State Medical Association.

OBITUARIES

DR. GERTRUDE M. JOHNSON

Dr. Gertrude M. Johnson died January 29, 1936, of lymphatic leukemia; aged 56 years.

Dr. Johnson was born in Minneapolis, Minn., December 12, 1879. She entered Battle Creek Sanitarium in 1898 in the School of Nursing, graduat-

ing in June 1900. She began the study of medicine in the American Medical Missionary College in 1900 and graduated in 1904, and since that time has been employed almost constantly as a member of the medical staff of Battle Creek Sanitarium.

In addition to her medical staff duties, she devoted time for several years to teaching in the School of Nursing. During her career in medicine she made two rather extended visits to Europe for postgraduate work, visiting both England and the Continent.

Dr. Johnson was a keen observer and diagnostician. In addition she devoted considerable time to research work, and produced several articles of value during the last few years. She completed a report on an interesting case during her last illness.

She was a member of the American Medical Association, of the Michigan State Society, of the Calhoun County Society, and also a Fellow of the American College of Physicians. She was greatly beloved by her patients, many of whom came to see her year after year because of the kindly interest she showed and the effort she made to neglect nothing that might afford them relief.

M. A. MORTENSEN, M.D., F.A.C.P.

DR. CARL FREDERICK MOLL

Dr. Carl Frederick Moll of Flint, Michigan, an Associate of the College since 1926, died suddenly of a heart attack in Detroit on May 1, 1936, at the age of 64 years.

Dr. Moll graduated from the Saginaw Valley Medical College in 1899, and started practice in the Upper Peninsula in Michigan. Shortly before the war, he moved to Flint, Michigan, and practiced as an internist in that city since that time.

Besides enjoying one of the largest practices in his city, Dr. Moll found time to give much to the medical organizations of the state and nation. He was Past President of the Marquette County Medical Society, and held numerous offices in the Michigan State Medical Society, including that of President. From 1926 to 1935, he was a member of the House of Delegates of the American Medical Association. His professional appointments were numerous. He was a member of the staff of St. Joseph's Hospital and of the Women's Hospital, as well as being President of the Staff of Hurley Hospital, and Physician to the Michigan Home of the Deaf.

Dr. Moll was well known both as an internist and as a citizen of the state. A man of warm friendliness and unselfish loyalty, he was well beloved by all of his fellow physicians, who will miss keenly his wise counsel and able leadership.

HENRY R. CARSTENS, M.D., F.A.C.P.,
Governor for Michigan

MINUTES OF THE GENERAL BUSINESS MEETING

DETROIT, MICH.

March 5, 1936

The Annual Business Meeting of the College was called to order at the Book-Cadillac Hotel at 5:00 p.m., Thursday, March 5, 1936, with President James Alex. Miller presiding.

Reading of the Minutes of the previous Business Meeting was dispensed with by resolution.

Dr. William D. Stroud, Treasurer, presented the following treasurer's report:

"At the present time our total funds amount to \$157,329.00. This is distributed into Endowment, \$58,281.72 and the General Fund, \$99,047.47.

"The funds have been audited and the accounts declared correct by a certified public accountant. Our investments as originally purchased, in bonds, amounted to \$111,844.00. Their present value, as of February 28, is \$116,430.00, or, in other words, they show a book profit of \$4,285.00.

"Our stock investments amount to a purchase price of \$14,811.00 and their book value at present is \$17,902.00, showing a profit of \$3,091.00. Our bonds and stocks have increased in value \$7,377.00 since they were purchased. I think this gives the members of the College a very secure feeling as to our finances."

The treasurer's report was accepted and filed.

Mr. E. R. Loveland, Executive Secretary, reported that up to this time 1,528 had registered at the Annual Meeting. He gave the following report on membership:

"During the past year 181 Fellows and 187 Associates were elected. That does not mean that the College has grown 368, because many of those elected to Fellowship were advanced from Associateship.

"During the past year, the Executive Offices had published the 1935 Directory containing the names of 5 Masters, 2415 Fellows and 818 Associates; total, 3238. Since the publication of the Directory on October 1, 1935, there have been 19 deaths, 10 resignations and 16 were dropped for delinquency (the number of resignations and the number dropped for delinquency was called to the attention of the general body, because the number was so small in comparison with the membership); 13 Associates were dropped for failure to qualify for Fellowship. With these elections and adjustments, the membership at this date was 4 Masters, 2565 Fellows and 843 Associates; total, 3412."

Mr. Loveland reported that since the rule has been in effect that new candidates must first become Associates and serve a probationary period of three to five years, over 75 per cent of such Associates had qualified for Fellowship. Of the class of Associates elected in 1931, 78 qualified for Fellowship and 23 failed for one reason or another. In other words, about 77 per cent of those elected in 1931 succeeded in becoming Fellows.

In regard to Life Members, he reported that there had been a further increase, the number having reached 61 to date. He referred to the Life Membership Roster being displayed at the College Booth near the registration headquarters.

Mr. Loveland further reported that a fairly large number of members visit the College Headquarters each year, and that in some instances he had been able to arrange programs of a medical character for visiting members, so that they could observe what is being done medically in Philadelphia. He invited members to visit the College Headquarters and to call on the College Offices for any assistance whatsoever that can be rendered. He thanked the members of the local Detroit committees who had helped so greatly in making the arrangements for the Detroit Session.

Dr. James Alex. Miller, President, on behalf of the Board of Regents, reported first upon the progress toward the establishment of an American Board of Internal Medicine for the certification of internists; that work had been organized under a joint committee of the American College of Physicians and the Section on the Practice of Medicine of the American Medical Association, the details having been worked out to such a point that the Board of Regents of this College had approved them, as far as the College was concerned, and the Committee was authorized to proceed. All that was necessary was the final approval of the American Medical Association, whereupon the Board will be ready to proceed with the regular installation of a method of certification of internists in this country. He expressed the prophecy that this will mean a long step forward in defining what internists really are and what specialists in Internal Medicine should be. He expressed the opinion that the work of this board will be of great help to the College in enabling it to make these examinations as a basic requirement for Fellowship. The work of this board will not in any way interfere with the activities of the College. Certification may be one of the requisites for admission to the College, but the College will undoubtedly always have other requirements for its Fellowship. This development will have a great influence in raising the standards of the practice of Internal Medicine in this country; the work of the College during the past year in sponsoring this board may be looked upon as of real significance.

The second subject discussed by President Miller concerned the finances of the College and various projects concerned therewith. He informed the members that over past years the College has been successful in accumulating a sum of money somewhat in excess of immediate needs. The Board of Regents has given serious consideration to this and has a definite program in mind, a program which in the future will enable the College to extend its usefulness and possibly at some future time to diminish definitely financial burdens of members, particularly in respect to initiation fees, which at present are \$80.00, having already been reduced from \$100.00. The College has been enabled to sponsor the American Board of Internal Medicine, because it had some available money. The College is going to finance all of the Board's work during the stage of its development, advancing the money until the Board is able to return it from the fees which will be exacted from those who take the examinations, and the College also has a plan of extending its other activities as it has financial opportunity to do so. Among these other activities may be the stimulation of clinical research among younger members of the profession by establishment of additional fellowships, also probably by the procuring of a suitable and dignified permanent home for the College. Furthermore, the Board of Regents has provided for the appointment of a committee to look into the details of other methods for the promotion of Internal Medicine. The procuring of a suitable home for the College will ensure permanency and add dignity to the organization. In conclusion, Dr. Miller expressed his appreciation of the coöperation the membership had shown in the arrangement of the Detroit Session, and for their interest and hearty coöperation during his term as President. He especially complimented the staff of the Executive Offices, the Executive Secretary, the Treasurer and the Finance Committee, stating it is due in no small measure to their efficient management that the College now finds itself in a position to expand somewhat in its field of usefulness in Internal Medicine. In conclusion he said in part:

"Now, personally, I wish to express again my own very deep feeling of appreciation of the great honor that you have conferred upon me in electing me to this office of President. It has been a year which has been most interesting and stimulating and one which I shall always remember with the greatest pleasure and which will always be a source of great satisfaction and will make me feel that, in being honored to be your President, there has been a year of productive effort and one of great satisfaction which I will always carry with me.

"I now come to a very pleasant duty as I lay down the responsibilities of the Presidential office. It is with very peculiar pleasure that I have the privilege of in-

ducting into office the incoming President. We have in our new President a man whom we all love, a man who is outstanding in his devotion to the best interests of the practice of medicine, a man who has given, both in the Board of Governors and in the Board of Regents, the best that he has to the interests of this College. We know what Ernest Bradley has been and, consequently, we are confident of what he will do for this College. It is therefore with the greatest pleasure and happiness, Dr. Bradley, that I turn over the responsibilities of this office to you." (Applause as all stand.)

President-Elect Bradley: "It really seems impossible that the time should ever come that I could stand here as your President, after the renowned men who have preceded me. Of course, to those other men who have been elected as President, it was just 'one other honor,' but to me, of course, without having had these honors, my friends down in Western Kentucky don't know whether I have been elected President of the American Medical Association, of some great medical university, or even of the United States. (Laughter.) It grieved my best friends to think that I had been elected the President of some great medical university, or that I would have to leave Lexington as President of the College of Physicians. I have tried to reassure them, so that if they get sick next year, they might come back to ask me about it.

"I have been thinking that, looking up at the altitude, at least, of these two former Presidents, Dr. Meakins and Dr. Miller, that if this thing keeps up very much longer going down like it is now, along about 1938 or 1939 you will be even below sea level as far as your President is concerned. (Laughter.)

"I couldn't possibly tell you, of course, really how great an honor this is to me. It is something, of course, I never dreamed of in my life. I just hope that I can do the best I can. I know that it will be difficult for any president to steer this old Ship of State very far wrong because if we make any mistakes or if we even shy off the course a little, we have a pilot on board all the time who will see to it that we don't go too near the rocks. I refer to Mr. Loveland, our Executive Secretary.

"I hope that with the coöperation of the members of the Society, which I know I will get, and the help of the Board of Governors and the advice of the Board of Regents, I will be able to carry on. I know that we have big things before us next year. The College is beginning to stand for more and more every year; it is becoming recognized more and more; and I cannot tell you how much I am honored by your electing me to this office. I thank you very much." (Applause.)

Dr. William Gerry Morgan, Secretary-General: "Dr. Miller, on behalf of the College, I have the privilege of presenting to you this token of our appreciation of your splendid accomplishments during your year as President." (Dr. Morgan presents the retiring President with an official gavel, appropriately engraved.)

Dr. Miller: "Mr. Secretary-General, Mr. President, Fellows of the College, it is a great pleasure to accept this symbol which is a symbol of an honor which has been conferred and which ever will be a memory of the great pleasure which I have had and which I have much enjoyed. I thank you again." (Applause.)

President Bradley called upon Dr. Pottenger, a member of the Nominating Committee, in the absence of the Chairman of that committee, Dr. Sydney R. Miller, for presentation of nominees for Officers, Regents and Governors, whereupon Dr. Pottenger presented the following nominations. The nominations for the elective offices had been published in the ANNALS OF INTERNAL MEDICINE, official journal of the College, more than thirty days preceding, in accordance with the By-Laws.

President-Elect James H. Means, Boston, Mass.
First Vice-President O. H. Perry Pepper, Philadelphia, Pa.
Second Vice-President David P. Barr, St. Louis, Mo.
Third Vice-President Walter L. Bierring, Des Moines, Iowa

BOARD OF REGENTS

Term Expiring 1939

James D. Bruce, Ann Arbor, Mich.
 Egerton L. Crispin, Los Angeles, Calif.
 James Alex. Miller, New York, N. Y.
 Francis M. Pottenger, Monrovia, Calif.
 Luther F. Warren, Brooklyn, N. Y.

Term Expiring 1938

Robert A. Cooke, New York, N. Y. (filling vacancy of the late Charles G. Jennings)
 Hugh J. Morgan, Nashville, Tenn. (filling unexpired term of James H. Means)

BOARD OF GOVERNORS

Term Expiring 1939

Oliver C. Melson, Little Rock, ARKANSAS
 Ernest H. Falconer, San Francisco, CALIFORNIA (Northern)
 Fred M. Smith, Iowa City, IOWA
 Joseph E. Knighton, Shreveport, LOUISIANA
 Henry R. Carstens, Detroit, MICHIGAN
 Edward L. Tuohy, Duluth, MINNESOTA
 A. Comingo Griffith, Kansas City, MISSOURI
 Robert B. Kerr, Manchester, NEW HAMPSHIRE
 Clarence L. Andrews, Atlantic City, NEW JERSEY
 Charles H. Cocke, Asheville, NORTH CAROLINA
 Julius O. Arnson, Bismarck, NORTH DAKOTA
 Alex. M. Burgess, Providence, RHODE ISLAND
 Kenneth M. Lynch, Charleston, SOUTH CAROLINA
 Paul K. French, Burlington, VERMONT
 J. Morrison Hutcheson, Richmond, VIRGINIA
 Charles E. Watts, Seattle, WASHINGTON
 Walter E. Vest, Huntington, WEST VIRGINIA
 D. Sclater Lewis, Montreal, QUEBEC

Term Expiring 1937

Walter W. Palmer, New York, NEW YORK (Eastern) (To fill unexpired term of Robert A. Cooke)

Upon motion by Dr. Meakins, seconded by Dr. Musser and unanimously carried, the nominees presented by the Committee were regularly elected.

President Bradley at this point expressed his appreciation of the manner in which Dr. James Alex. Miller had conducted the office as President during the past year, the way the College had been run and the kindness of the retiring President for his advice. Dr. Bradley expressed his keen approval of the plan of having a man serve one year as President-Elect, so that he may become more familiar with the needs of the College and the means of accomplishing those needs before he is inducted to the presidency. He asked for suggestions from members at large, from the Governors, the Regents and other Officers, during the year.

On motion by Dr. Pincoffs, seconded by several and unanimously adopted by a standing vote, it was

RESOLVED, that the American College of Physicians express its deep appreciation to all local agencies, including the Wayne County Medical Society, local committees, the local profession, the Convention Bureau, the Book-Cadillac Hotel, the committees at Ann Arbor

and the University of Michigan for their aid and coöperation in the conduct of its Twentieth Annual Session.

Adjournment.

Attest: E. R. Loveland,
Executive Secretary

MINUTES OF THE BOARD OF GOVERNORS

DETROIT, MICH.

March 2, 1936

The first meeting of the Board of Governors of the American College of Physicians, held in connection with the Twentieth Annual Session, Detroit, Mich., was called to order at 5:25 p.m., March 2, 1936, at the Book-Cadillac Hotel.

In the temporary absence of the Chairman, Dr. Charles H. Cocke, Dr. C. W. Dowden acted as Chairman pro tem. The Executive Secretary called the roll, with the following present: Dr. Oliver C. Melson, Dr. Tom Bentley Throckmorton, Dr. Joseph E. Knighton, Dr. James D. Bruce, Dr. Edward L. Tuohy, Dr. A. Comingo Griffith, Dr. Clarence L. Andrews, Dr. Julius O. Arnson, Dr. Alexander M. Burgess, Dr. J. Morrison Hutcheson, Dr. Charles E. Watts, Dr. Walter E. Vest (representing Dr. John N. Simpson), Dr. D. Slater Lewis, Dr. Fred W. Wilkerson, Dr. Turner Z. Cason, Dr. Glenville Giddings, Dr. C. W. Dowden, Dr. Edwin H. Gehring, Dr. Louis H. Fligman, Dr. Robert A. Cooke, Dr. A. B. Brower, Dr. T. Homer Coffen, Dr. Charles T. Stone, Dr. Ramon M. Suarez, Dr. James F. Churchill, Dr. Gerald B. Webb, Dr. Wallace M. Yater, Dr. Ernest E. Laubaugh, Dr. Cecil Jack (representing Dr. Samuel E. Munson), Dr. Robert M. Moore, Dr. Thomas Tallman Holt, Dr. Allen A. Jones, Dr. Leila Andrews (representing Dr. Leander A. Riely), and Dr. Louis E. Viko.

Mr. Loveland then read abstracted Minutes of the last meeting of the Board of Governors, which, upon resolution, were approved as read.

Dr. Walter L. Bierring, Chairman of the Committee on the Certification of Internists (American Board of Internal Medicine) distributed copies of the articles of incorporation, the Constitution and By-Laws of the proposed American Board of Internal Medicine, and discussed at length the proposed organization of this board. The details of the discussion are not repeated here, since they are duplicated in the Minutes of the Board of Regents.

Dr. Dowden called upon the Executive Secretary to present communications. Aside from those from Governors who were unable to be present, Mr. Loveland read one from Dr. Adolph Sachs, Governor for Nebraska, in which Dr. Sachs suggested the desirability of changing the method of electing Governors. The present By-Laws provide that a Nominating Committee appointed by the President shall, after consultation with members in the various States to be represented, prepare a slate of nominees for the Board of Governors. Dr. Sachs' recommendation was that Governors shall be elected by their local constituents.

On motion by Dr. Vest, seconded by Dr. Giddings and regularly carried, it was

RESOLVED, that the Chairman shall appoint a Committee to investigate the proposal of Dr. Sachs concerning the election of Governors and report back at the next meeting of the Board.

Dr. Dowden requested from the Executive Secretary a report on the elections to Fellowship and Associateship that had been made March first by the Board of Regents. Mr. Loveland reported that the list of elections had been posted on the Bulletin Board and that it included the full list of candidates elected both to Fellowship and to Associateship. He offered to read the names to any who had not examined the list on the Bulletin Board.

On motion by Dr. Griffith, seconded by Dr. Melson, and regularly carried, it was

RESOLVED, that the list of candidates, both for Fellowship and Associateship, as elected by the Board of Regents, be approved by the Board of Governors.

The Executive Secretary, Mr. Loveland, then reported upon the names of members who had been dropped from the roster for various reasons, including failure to take up membership within one year after election.

At this point, Dr. Charles H. Cocke, Chairman of the Board of Governors assumed the Chair.

Mr. Loveland proceeded with his report, distributing to members a list of those Fellows and Associates from each State who were subject to being dropped because of more than two years' delinquency. He also distributed an outline of the Associates elected at the 1931 Session whose names were being dropped for failure to qualify for Fellowship. The Governors were asked to take the lists with them for future reference. Mr. Loveland pointed out that out of a membership of something over 3300 only 16 were dropped for delinquency, a very gratifying record. Members of the Board of Governors were requested to make any suggestions concerning any names on the list, with the understanding that the Board of Regents would be glad to do anything reasonable if any mistakes had been made in dropping any of the members.

Dr. Cocke, as Chairman, thanked the Board cordially for their coöperation and for the very excellent attendance at this meeting, for the faithfulness with which they have done their work, and particularly for their care in responding to his various communications. Dr. Cocke reported that since the last meeting, the College had lost through death one Master, 32 Fellows and 6 Associates. He also read the list of new Life Members added since January 1, 1936, including the following.

Lewis Beals Bates, Ancon, C. Z.
Casper H. Benson, Columbus, Ohio
Donald Gregg, Wellesley, Mass.
James Rae Arneill, Denver, Colo.
Thomas Fitz-Hugh, Jr., Philadelphia, Pa.
C. Charles Burlingame, Hartford, Conn.
Noble Wiley Jones, Portland, Ore.
Cecil M. Jack, Decatur, Ill.
Anna Weld, Rockford, Ill.
Roy M. Van Wart, Descanso, Calif. (formerly of New Orleans)
Estes Nichols, Portland, Maine
William Henry Watters, Coconut Grove, Miami, Fla.

Dr. Cason, Governor for Florida, presented the matter of the time of the Annual Meeting. He had been requested by several of the members in Florida to present a resolution asking for the postponement in the date of the Annual Meetings to a later time in the year. Dr. Cason had had communications from practically every member in Florida. Some of them were unable to come because of the press of work, this being the busiest time of their season. Furthermore, the character of the winter in the North in March was such as not to attract members from the warmer climates.

Chairman Cocke explained that the date of the meeting is usually set by the local committee on arrangements in accordance with the necessities of their local conditions, schools, hospitals, etc. He offered to entertain a motion, however, for presentation to the Board of Regents.

On motion by Dr. Cason, seconded by Dr. Churchill, and regularly carried, it was

RESOLVED, that the Board of Governors recommend to the Board of Regents and such other Officers as may be concerned in the selection of the time for the Annual Meeting to hold future Annual Sessions at as late a date in April as consistent with the convenience of those in the city in which the meeting will be held.

At this point Chairman Cocke brought up the question of alternates for members of the

Board of Governors who may be unable to be present at the annual meetings. The By-Laws make no provisions. The matter had already been brought to the attention of the Board of Regents on the previous day, and that Board had given authority to the Board of Governors, as they see fit, to accept the proxies of absent Governors who were unable to attend this particular Session, and to accept their substitutes to act in their full stead and to enjoy all their full rights under the Constitution. For this reason, Dr. Walter E. Vest, of West Virginia, was acting in the stead of Dr. John N. Simpson; Dr. Cecil Jack, from Southern Illinois, was acting in the stead of Dr. Samuel E. Munson; and Dr. Leila Andrews, of Oklahoma, was acting in the stead of Dr. Leander A. Riely.

On motion by Dr. Dowden, seconded by Dr. Cason, and regularly carried, the seating of the above alternates was approved.

On motion by Dr. Griffith, seconded by Dr. Giddings, and regularly carried, it was

RESOLVED, that the Board of Governors suggest to the Board of Regents the desirability of having the By-Laws amended to provide for the appointment of alternates for Governors who cannot attend the Annual Sessions.

Chairman Cocke then read a communication from Dr. Henry M. Thomas, Jr., Governor for Maryland, discussing the ultimate future of the College, and suggesting ways and means of approaching the chiefs of various important medical services concerning promising younger members of their staffs for Associateship.

Chairman Cocke pointed out that as soon as the American Board of Internal Medicine begins to operate, there may be certain changes necessary in the way candidates may become Fellows of the College. At present, except in very exceptional cases, new candidates must be presented first for Associateship. After the new Board is operating and a physician is certified as an internist by that Board, it will form the ground work or the foundation or the presumption of his eligibility for admission to this College, although there will be several other requirements.

Chairman Cocke asked for suggestions or ideas which he might transmit to the Board of Regents for their consideration.

Chairman Cocke proceeded to the matter of the reinstatement of old members, reporting upon two cases that had been liberally discussed by the Board of Regents the day before. If a man voluntarily resigns and is out of the College for a given period of time, it matters not whether it is a year or ten years, the Regents are disposed to require him to come back either through the regular channel of reelection or on the recommendation of the Governor for his district and the payment of all past dues. Members having voluntarily eliminated themselves by resignation do so on their own responsibility, and the College should not waive their requirements and allow a man the privilege of resigning and coming back at will. Such action would create a hopeless situation with men dropping and taking up their memberships constantly.

Dr. Holt, Governor for Kansas, inquired concerning the effect of new changes that would be brought about by the operation of the American Board of Internal Medicine.

Chairman Cocke informed the Board that until the Constitution and By-Laws have been amended candidates will continue to come in under the present arrangement. It is quite certain, however, that amendments will be adopted as soon as the Board is ready to operate, and that thereafter new candidates will be subject to the new requirements.

Dr. Burgess, Governor for Rhode Island, wished further discussion of the matter of reinstatement of members, presenting an illustrative case of a member stricken with pulmonary tuberculosis, or some other illness, making it necessary for him to retire from active membership in his societies. Such a man might later recover and desire to be reinstated.

Chairman Cocke replied that there was no need for such a man resigning, that the By-Laws provide that in the case of protracted illness and retirement from practice, a member is entitled to appeal to the Board of Regents for a waiver of his dues during such period. The Board of Regents, in accordance with the By-Laws, are considerate in such cases and, hence, no member needs to sacrifice his fellowship in the College because of his health. Upon a member's recovery and resumption of practice, his status changes to that of a paying

member, and in the meantime there is no necessity for reinstatement because he has remained a member all the time.

Dr. Moore, Governor for Indiana, reported on College membership in his State. In that State it has appeared difficult to procure men who are doing wholly Internal Medicine in any given smaller city. Many of the men in these cities who would be interested in the College, however, do restrict their work to 90 per cent or 95 per cent Internal Medicine. However, some of these are doing, to some degree, minor surgery and handling an occasional obstetrical case. Many of these men are interested in College membership, though the question has existed as to whether they are qualified under the circumstances.

Chairman Cocke suggested to Governor Moore that such men might properly be proposed for an Associateship. Candidates limiting their work almost wholly to Internal Medicine may be considered eligible for Associateship, with the understanding that before they come up for Fellowship they will probably be able to limit their work wholly.

Chairman Cocke then informed the Board of Governors concerning the details of the discussion in the Board of Regents concerning the procuring of a College Headquarters or permanent home. Quoting from his remarks: "The headquarters is located in a singularly small and inadequate suite of offices at 36th and Walnut Streets in Philadelphia. During the incumbency of Mr. Loveland as Executive Secretary, the funds of the College have increased remarkably, namely, from approximately \$9,000 to \$158,000. It has been the thought of many of the Regents that since this fund has been raised without specific, definite, planned ideas for its distribution, or its use, although the College has used a certain amount for awards, for scholarships and that sort of thing, and while the College will continue to foster those projects, the time has arisen when the College must have more adequate, better and larger facilities, through the building or acquisition of a suitable home. . . . Those who were present at the Regents-Governors Banquet last evening, March first, heard the discussion presented so well by Dr. Alfred Stengel, Chairman of the Temporary Committee appointed to look into the feasibility of this project. I would be very happy to have any reaction or any remarks from any Governor present as to his feeling or thoughts of his constituents toward this possibility. Of course, a natural corollary of that would be that there would be some reduction either of the dues, or, more particularly, of the initiation fee once a permanent home has been acquired."

Dr. Yater, Governor for the District of Columbia: "Mr. Chairman, certainly there is no question as to the advisability or the necessity of such a permanent headquarters. It is perfectly ridiculous that such an organization as this should not have had one long since. Furthermore, with all the troubles brewing in our country at the present time and the possibilities of inflation, and what not, if we wait, say a year or so, to feel out the consensus of opinion of the majority of our members, we shall be losing very valuable time and money, because a year from now very likely the property which we can now obtain for a certain figure will probably cost much more and construction will be more expensive. This would seem to me also to be a very important consideration in the investment of our funds. In order to bring the matter to a point of discussion, I would move, Mr. Chairman, that the Board of Governors shall express to the Board of Regents their approval of the project for the acquisition of a permanent College home and headquarters, and, further, that the Board of Regents proceed immediately on the project."

The motion was seconded by Dr. Griffith, Governor for Missouri.

Dr. Bruce, Governor for Michigan: "I can't resist the temptation to tell you all how gratified I have been personally and how gratified the members of Michigan have been with the progress of the College, and I am perfectly sure that I am expressing their wishes in supporting the motion that has been made. They will be very happy if this can be carried through."

Dr. Tuohy, Governor for Minnesota: "I am glad to voice the opposition and to elaborate on what I have already said. I think it is quite obvious that you are going to have this building, but I shall appreciate, nevertheless, if you will bear patiently with me for a moment while I attempt to clarify my position. I believe the American College of Surgeons has

added nothing to the prestige of that organization, or to the advancement of the purposes for which they were originally established, by the acquirement of their home. I want to clarify the matter as to the centralization in Philadelphia. I think the advisability of that has been well proved by the success that has come to the College since the work was centralized, and so I think there is, in fact, no argument pertaining to that feature. Philadelphia is a happy choice, both from the standpoint of traditions of medicine and the first hospital and the first medical school established in the United States. If the College Headquarters were developed in Washington, near the Surgeon General's Library, I think the advantages would be of little moment in comparison to the equal advantages that exist in Philadelphia."

Dr. Tuohy proceeded to ask for a consideration purely on a business basis, and pointed out that the College funds could be invested in other than United States securities, if inflation is threatened. He recommended careful consideration of renting more space in Philadelphia as a comparison with the cost of maintaining a College Headquarters. He questioned whether a College home would be considered by the members at large of any value. He recommended various methods of extending the sphere of influence in the College into various sections of our country, including regional convocations with the purpose of instilling better Internal Medicine into the various States and Provinces. He further pointed out that the Royal College of Physicians has given little attention to its housing. He urged no hasty action until the matter had been duly considered.

Dr. Holt, Governor for Kansas, also spoke to the question, and Dr. Cason, Governor for Florida, insisted on some word from the Executive Secretary from the standpoint of a business man who may thoroughly understand the facts of the case, because of his closeness to the College.

Chairman Cocke replied that the progress thus far had been carried on not only with the advice and coöperation, but with a very active interest of the Executive Secretary, but that the Executive Secretary had expressed a preference not to enter too actively in the discussion of the matter. However, he called upon Mr. Loveland to make some remarks to the inquiries.

Mr. Loveland pointed out, first, that the matter of the College Headquarters is one to be settled by the College. A committee had been formed which had called upon the Executive Secretary to determine certain information and to make certain surveys, report on which had been presented by Dr. Stengel. He said he was favorable to the project; second, the College by conservative operation and care has accumulated a considerable surplus, which is likely to be dissipated with an increasing interest in other projects and probably through changing personnel on the various Boards. The By-Laws provide for a certain amount of change in members of the Boards, and without disparaging the good intent of any one, the investment of a certain part of the surplus in some worthy problem, such as an appropriate and dignified home for the College would be a safeguard. However, the chief consideration was the actual need of larger and more adequate quarters. Many members of the College visit the College Offices every year and frequently express disappointment in the rather small and inadequate quarters. The efficiency of the College work is somewhat hampered by inadequate facilities. He said he would not recommend an extravagant building, but something fairly modest, of attractive architecture and of reasonable proportions for present and future work of the College. In his opinion a permanent headquarters would contribute toward stability. These surplus funds might readily be used, if not for a College Headquarters, for other purposes that may be far less enduring. Adequate quarters would make it possible for members of the College to come to Philadelphia and use them for their headquarters, where mail could be sent, consultations held, and so on. The College, further, could operate better with its members in arranging programs to see what is being done medically in Philadelphia, or for postgraduate study. The headquarters might also be used for the giving of examinations by the American Board of Internal Medicine, after its formation. It is also possible that some other medical group or groups might use, on rental from the College, any excess space available for their own offices.

Dr. Griffith, Governor for Missouri: "I want to go on record as saying that I am for

this proposal all the way through. I do not think the American College of Surgeons and the American College of Physicians should be compared. One is a huge organization with many members and different branches all over the country. Ours is a real fellowship organization. We have a smaller, more limited number of members. I think we are an organization that should have a permanent home, a place to which we can point with pride. I am not in favor of Washington. That location would be all right if we were a larger political organization and wanted to get something out of the Government. As to inflation, whether we have stocks or bonds, we are drawing a certain interest from our money. The dollar is now worth only fifty-nine cents, and if we have further inflation, no one knows what its worth will be. If we have real property, we shall have something tangible, and the value will be there."

Dr. Suarez, Governor for Puerto Rico: "This is the first meeting of the Board of Governors that I have attended, and I have been most favorably impressed by the things I have heard. It took me six days to get to this meeting, and I cannot resist the temptation to say at least a few words about the building of a permanent home for the College. I have been President of the Puerto Rico Medical Society for three years, and during my incumbency, a beautiful home for the medical profession of the Island has been built. We are proud of it and we think it is one of the best things we could have done for the medical profession there. I frankly and firmly believe that the construction of a permanent home for the American College of Physicians would be a most definite sign of permanency and stability, and I see no reason why, since we have progressed so wonderfully since our headquarters were established in Philadelphia, the new building shouldn't be constructed also in that City."

Dr. Giddings, Governor for Georgia: "It seems to me that it is practically essential for this College to have a headquarters. Certainly if this examination and certification of internists is passed and put into operation, the necessity of such a headquarters will be even greater. I rather feel that we not only should have a home, but that the place should be fireproof, and I rather question whether such a structure can be erected for the sum that has been suggested."

Dr. Moore, Governor for Indiana: "I want to be on record as for this project. I feel favorable toward establishing a permanent home. As to other projects of the College, I am well acquainted with fellowships. I have observed many fellowships established to help students through school. It doesn't make a bit of difference whether it is a fellowship from the American College of Physicians or some other organization. Most of the money spent on these fellowships is soon gone and forever forgotten. If we have something substantial to which we can point, I think it will bring prestige to our organization, as it should. It doesn't make any difference whether it is your own office or the headquarters of your organization. If you have a poor office, it doesn't impress your visitors favorably. An organization of our standing and our honor, I think, can have nothing but the best."

Chairman Cocke put the motion to a vote, whereupon the resolution was unanimously adopted.

RESOLVED, that the Board of Governors shall express to the Board of Regents their approval of the project for the acquisition of a permanent College home and headquarters, and, further, that the Board of Regents proceed immediately on the project.

At this point, Chairman Cocke introduced the President of the College, Dr. James Alex. Miller. (Applause.)

President Miller: "It is particularly a pleasure to be here and to get the reaction of the Board of Governors on this conception which has arisen in the Board of Regents, and I can tell you that your reaction taken this afternoon will have very great weight in determining the action of the College through the Board of Regents, where, of course, the responsibility lies. I also want to say that at our meeting last night, it was a great pleasure to us of the Board of Regents to be your hosts. That dinner was not a College affair, but was a spontaneous and personal invitation on the part of the members of the Board of Regents to the members of the Board of Governors, expressing the personal anxiety of the former to get

closer to the Governors. That was the basis on which that meeting was held, and which I hope will be a precedent for similar meetings. I also want to say that during this last year, over which it has been my privilege to preside as your President, I have been more and more impressed with the importance of the Board of Governors individually and collectively in the affairs of this College. Of course, we have our Constitution and By-Laws; certain prerogatives, certain details and privileges are assigned to the Board of Regents and others to the Board of Governors, but we are all cognizant that it is the personnel of the College which counts, and it is there that the Board of Governors must take the initiative. I feel so strongly about this that I have made it the practice during the last two or three years not to exercise as Regent my prerogative to certify or to endorse candidates. I think that under certain exceptional circumstances, perhaps, it is wise to allow a Regent to endorse a candidate, but I have made it an invariable rule when proposals have been sent to me to refer them to the Governor of my district, in order that they may go through the regular channels of the Board of Governors, because I believe the responsibilities should rest with them; and I believe it is up to you, gentlemen, to exercise as you have in the past, but even increasingly in the future, a good deal more of a sense of responsibility in passing upon the credentials of candidates whose proposals you pass to the Committee on Credentials. It is not fair or right to send a doubtful candidate's proposal to the Credentials Committee; you usually have available first-hand information, whereas that Committee does not, and if they do not receive it, they cannot act in the best interests of the College. . . .

"I also think that you should insist more and more upon discretion on the part of Fellows who present candidates to be endorsed by you. We must have greater local autonomy, or at least a greater local sense of responsibility toward the problems of the College.

"I, too, feel as you, gentlemen, have expressed it, that we will go far, if we have our permanent home, toward increasing the feeling of pride and stability in our organization, which I think is extremely important. An even more important step is that which we are making on the question of the certification of internists, which, when it is consummated, will make it quite possible for us to use that examination instead of the preliminary stage of Associateship. That is not yet an assured fact, but is being considered in that connection. You should understand that it is not the idea of the present Board of Regents that this certification will in any sense qualify an individual for Fellowship. It will simply give him the basic minimum requirement; and in the future, I hope, no one who is not certified as an internist will be even considered by our Credentials Committee. After that, we can add any particular requirement and essentials that we think wise. I feel sure we are just ready for a move forward for this organization which is going to make it a great power, not only from the standpoint of the standards of practice, but also in the standards of qualification for certain types of practitioners, specialists, if you want to call them such. I hope we shall also have an opportunity to exercise great influence on ethical standards, which are tremendously necessary. I think we may be very proud of the leading part that the College has taken in this matter. Thank you very much for the privilege of speaking to you." (Applause.)

On motion by Dr. Griffith, seconded by Dr. Yater, and adopted by a unanimous rising vote, it was

RESOLVED, that the Board of Governors express to the members of the Board of Regents their keen appreciation and thanks for the Dinner tendered them on March 1.

Adjournment.

Attest: E. R. LOVELAND,
Executive Secretary

MINUTES OF THE BOARD OF GOVERNORS

DETROIT, MICH.

March 5, 1936

The second meeting of the Board of Governors of the American College of Physicians, during the Twentieth Annual Session, was held Thursday, March 5, at the Book-Cadillac Hotel, with Dr. Charles H. Cocke, Chairman, presiding, and with the following present: Dr. Oliver C. Melson, Dr. Tom Bentley Throckmorton, Dr. Joseph E. Knighton, Dr. James D. Bruce, Dr. Edward L. Tuohy, Dr. A. Comingo Griffith, Dr. Clarence L. Andrews, Dr. Charles H. Cocke, Dr. Alexander M. Burgess, Dr. J. Morrison Hutcheson, Dr. Walter E. Vest (representing Dr. John N. Simpson), Dr. D. Sclater Lewis, Dr. Fred W. Wilkerson, Dr. Turner Z. Cason, Dr. Glenville Giddings, Dr. C. W. Dowden, Dr. Edwin W. Gehring, Dr. G. W. F. Rembert, Dr. Louis H. Fligman, Dr. A. B. Brower, Dr. T. Homer Coffen, Dr. Charles T. Stone, Dr. James F. Churchill, Dr. Gerald B. Webb, Dr. Henry F. Stoll, Dr. Wallace M. Yater, Dr. Ernest E. Laubaugh, Dr. Cecil Jack (representing Dr. Samuel E. Munson), Dr. Robert M. Moore, Dr. Leila Andrews (representing Dr. Leander A. Riely), Dr. Louis E. Viko and Dr. Jabez Elliott, and E. R. Loveland, Executive Secretary, acting as secretary of the meeting.

By resolution, the reading of the Minutes of the previous meeting was dispensed with.

Chairman Cocke reported to the Board upon matters he had been instructed to refer to the Board at a previous meeting:

(1) The resolution urging the Board of Regents to proceed toward the acquisition of a College Headquarters was favorably received and spread upon their Minutes.

A new committee was appointed by the President to take the matter in hand, with instructions to bring in definite and concrete specifications as to location, type of building, etc., at the next meeting.

(2) The resolution containing recommendation for amendments to the By-Laws providing for appointment of alternates for Governors who cannot attend the Annual Sessions was approved, and the Committee on Constitution and By-Laws instructed to draw up proper amendments.

(3) The resolution requesting a later date for the Annual Sessions was received and given due consideration, with the result that the 1937 meeting will be held later in the year than customary.

At this point, Chairman Cocke called upon a special committee previously appointed to consider the suggestions of Dr. Adolph Sachs, Governor for Nebraska, for a new method for election of Governors. The following report was received:

"The Committee appointed by you to consider the suggestions made by Dr. Adolph Sachs, Governor for Nebraska, namely, 'that in the future the Governor for each State shall be elected by the Fellows in his respective State or district,' met Wednesday afternoon, March 4, 1936, and, after due deliberation, unanimously recommends that there be no change in the present method as provided in the By-Laws, for the following reasons:

"First, under the present efficient method carried out under the By-Laws, the College has advanced and thrived without any type of dissension.

"Second, your Committee is quite fearful that if the election of Governors be left to the decision of Fellows in the respective States, politics might readily enter.

"Respectfully submitted,

C. L. ANDREWS,
F. W. WILKERSON,
A. C. GRIFFITH, *Chairman*"

On motion by Dr. Knighton, seconded by Dr. Yater, and regularly carried, it was RESOLVED, that the Board of Governors adopt the above report.

Chairman Cocke reported that while the final amendment would specify the method of appointing alternates, it was his understanding that the power of appointing an alternate would be vested in the local Governor, who should certify to the Executive Secretary the appointment of his alternate, and should give a letter of appointment to the alternate himself.

The Executive Secretary, Mr. Loveland, distributed copies of the financial report of the College for 1936. He reminded the Governors that while the Board of Regents is responsible for the business operation of the College, it is desired to keep the Governors also informed. He reminded them that the accounts of the College are audited each year by a certified public accountant. He reviewed the various parts of the report, summarized the operating statements and explained the General and Endowment Funds. The financial reports have been published in connection with the Minutes of the Board of Regents, and are not here repeated. There was general discussion about the various statements, and a keen interest displayed by members of the Board.

Dr. Throckmorton, Governor for Iowa, called attention of the Board of Governors to the income from the annual exhibits, as shown in the statement. He stated that that was one of the first things which struck his attention, because of his own experience with exhibit work in his State society and in some national organizations. He pointed out that the success of these exhibits represents an unusual amount of work carried on by the Executive Offices, and it should be deeply appreciated by the College. He added, "I know from personal experience that it takes a lot of good hard work not only to get exhibitors, but after having gotten them to keep them satisfied and to keep them coming, and for that reason I personally want to compliment the Executive Secretary and his staff upon that unusual work which they have done in this particular line. It shows in the income that it is a mighty fine thing for the College. I would call your attention to the fact that this activity accounts for a considerable part of the surplus which may be used for the acquiring of a College home and other activities. I want to say that this surplus came largely from the sweat of the brows of the Executive Secretary, the Finance Committee and the Regents, and there is nothing unworthy about it at all."

Chairman Cocke pointed out that the commercial exhibits before the College meetings are carefully censored, and an earnest effort is made to admit only the most ethical and reliable products.

Dr. Vest reported that his examination of the exhibits had shown that nothing in the exhibit was worthy of criticism in any way. They were all proper exhibits.

The Executive Secretary then reported upon the publication, during the autumn of 1935, of a new Directory of the College. He called attention to the revised arrangement of data, and expressed the hope that the usefulness of the Directory would be greatly extended. Mr. Loveland further reported on the new Life Members of the College, totalling now 61 in all; he reported on the elections to Fellowship and Associateship and gave the membership statistics. By resolution, the report of the Executive Secretary was accepted.

The Executive Secretary presented for the advice of the Board of Governors the problem of whether or not there should be published in the Directory the names of all Associates as well as the Fellows, as done at the present time. As a matter of fact, Fellows and Masters only are "members" in the true sense of the word, since Associates do not have the power to vote, nor is the Associate roster a permanent one. Associates of the College in general may be divided into three groups: (a) those who first entered as members of the American Congress on Internal Medicine and were automatically given the status of Associates when the said Congress was merged with the College in 1926; (b) men elected to Associateship after meeting definite requirements for the same between 1926 and 1929; (c) Associates elected since 1929 who are under obligation to qualify for Fellowship within a maximum period of five years from election to Associateship. The first two groups may remain Associates indefinitely, because the amendment to the By-Laws requiring qualification

for Fellowship by Associates only began to apply in 1929. Suggestions had been received in the College office that possibly the official Directory of the College, upon which members of the College are judged, should include only full-fledged Fellows.

Chairman Cocke requested a discussion of the matter.

Dr. Bruce, Governor for Michigan, after discussing the matter, summarized his opinions by saying that he felt we are perfectly able to vouch for all the Associates who have been elected since 1929, because they were compelled to meet certain definite requirements, and unless they succeed in qualifying for Fellowship, their names automatically will be dropped. For the earlier group of Associates who were brought into the College automatically, he felt some provision should be made so that they could be distinguished from the rest of the Associates.

On inquiry from Dr. Dowden, Governor for Kentucky, it was brought out that the American Medical Association in its Directory does not recognize as members of the College others than Masters and Fellows. Dr. Dowden expressed the opinion that Associates might be omitted from the Directory, so that confusion of Associates as full-fledged members might be obviated.

Dr. Knighton, Governor for Louisiana, expressed his gratitude for having the various classes of Associates clearly defined. He continued to report upon a sectional meeting of the Fellows and Associates of the College in the form of a combined clinical and social meeting in Shreveport during January, 1936. The membership especially represented was that of northern Louisiana. Dr. Knighton reported a very successful meeting with full attendance, lacking two, in that entire territory, and with additional meetings planned for the future.

Returning to the matter of the College Directory, Governor Griffith suggested that Associates of the College granted by virtue of membership in the old American Congress on Internal Medicine should be published separately, or under special designation.

Dr. Jabez H. Elliott, Governor for Ontario, concurred in this suggestion. Dr. Elliott said that it should be a question for discussion whether the College should carry the Associates in the Directory at all, because of the confusion in the minds of certain people as to whether or not they are full members of the College. However, if the Associates shall be published, then those who were admitted previous to the establishment of definite admission requirements should be set apart.

Chairman Cocke pointed out the condition should be corrected in the next Directory, but inasmuch as the next Directory will not be published until 1937, the intervening time might be used for more mature thought and for definite action at the next meeting. Dr. Cocke suggested that perhaps one of the means of handling this situation would be to have a full official Fellowship Directory of the College and to issue a supplementary Directory of Associates. The official Fellowship Directory would be the one distributed to libraries, medical schools and other official institutions.

Dr. Vest suggested that in our Directory we should publish only the Fellows and a list of "eligibles." This eligible list would include only those who are eligible for advancement to Fellowship, and would eliminate the names of all those who have not met the preliminary requirements for Fellowship.

President Bradley, at the request of Dr. Churchill, explained that the American Congress on Internal Medicine and the American College of Physicians were founded as two separate organizations. The first essential to be a member of the American Congress on Internal Medicine was merely a desire to attend its meetings and to pay an admission fee of \$5.00. There were always requirements for admission to the College. However, the meetings of the College and Congress were held together, and members of the College were recruited more or less from members of the Congress. When the Congress was discontinued, its members were accorded Associateship in the American College of Physicians.

Dr. Brower, Governor for Ohio, inquired how many such Associates still remain on the list and what is their average age. An examination of the list by the Executive Secretary

indicated there are 173, whose average age is 57 years. Ten of these are 65 years of age or older, and, therefore, on the dues-waived list. The balance pay the regular Associateship dues.

Dr. Moore, Governor for Indiana, and Chairman Cocke both concurred in the opinion that this Directory is being used by hundreds of physicians who are not members and by hosts of physicians who do not attend the Sessions of the College. It is not infrequently that the Directory is used for reference for physicians to whom patients may be referred because of the removal of such patients from one part of the country to another, or because of travel. They expressed the opinion that the Directory should contain only the names of physicians whose credentials are of high grade.

Dr. Andrews, Governor for New Jersey, expressed the opinion that the College is under some obligation to this earlier group of Associates, because of the original agreement to grant them Associateships.

Dr. Hutcheson, Governor for Virginia, suggested that Fellows be given complete geographic and alphabetical listing, but Associates be listed alphabetically only in the back section of the Directory.

Dr. Holt, Governor for Kansas, expressed the opinion that the obligation of the College to these early Associates is such that their regular listing should be maintained.

Dr. Ernest B. Bradley, President-Elect of the College, at this juncture was called upon to address the Board of Governors briefly, asking them for their suggestions, aid and co-operation during the coming year, the term of his Presidency.

Chairman Cocke opened a discussion of regional or State meetings of members of the College. He expressed the opinion that the objects of these are (1) the establishment of greater coherence among the Fellows; (2) building up of more local pride in Fellowship; (3) dissemination of a better understanding of what the ideals and purposes of the College are; and (4) the furtherance of wider acquaintanceship and better fellowship among the members.

Dr. Cocke reported that during the past year he had attended two of the State meetings, one in Kentucky and one in his own State of North Carolina. He had had reports from several Governors who had conducted such meetings in their territories. These meetings should be conducted by the Governor, and in some instances may be joint meetings among two or three neighboring States where the membership is smaller and the cities not too far removed from one another.

Dr. Griffith, Governor for Missouri, announced that during the meeting of the American Medical Association in Kansas City during May some attempt will be made toward having a social meeting of members of the College from that community. He extended a cordial invitation to all members of the Board of Governors, Board of Regents and members of the College to be there.

Dr. Yater, Governor for the District of Columbia, recommended that the College office should maintain up-to-date records about all of the members of the College, new honors, new positions, new publications, etc. He said there should be some one place in the country where internists shall have available a complete up-to-minute record of the medical histories of the outstanding men. Each year a form could be sent out by the Executive Secretary to all of the Associates and Fellows, probably more importantly to the Associates, asking them to put down changes in their status in their respective communities, new positions they are holding, outline of articles they have written, outline of papers they have delivered before national organizations, etc. This might also be quite a stimulus to Associates who must prepare their credentials for Fellowship by inquiring each year what they have accomplished during the preceding year. They will be reminded and given a stimulus toward better qualifying themselves for Fellowship.

On motion by Dr. Yater, seconded by Dr. Andrews, and regularly carried, it was

RESOLVED, that the Board of Governors suggest to the Board of Regents that each year the Executive Secretary send out appropriate questionnaires to obtain information as to the

status and work that members of the College have done during the preceding year, and that these records shall be kept on file in the headquarters office.

On motion by Dr. Giddings, seconded by Dr. Yater, and regularly carried, it was

RESOLVED, that the Board of Governors draw up resolutions expressing its very deep sympathy for the family of Dr. Charles G. Jennings and also for the family of Dr. Frederick Epplen. (Secretary's note: Dr. Charles G. Jennings, deceased, was General Chairman of the Twentieth Annual Session at Detroit, 1936, a Master of the College, and for many years Chairman of the Board of Governors; Dr. Frederick Epplen, deceased, was for many years Governor for the State of Washington.)

Dr. Andrews, Governor for New Jersey, expressed his disappointment that the Daily Bulletin had been discontinued at the current Session. He expressed the opinion that many other members were likewise disappointed. It served as an aid in locating members of the College who were in attendance at the meeting and as a guide to the happenings of the current day.

The Executive Secretary, Mr. Loveland, explained that the Daily Bulletin had been discontinued primarily because of the expense of publication and the amount of work entailed. The Daily Bulletin had to be printed at night. The burden fell upon the Executive Secretary's office because there was no one else available to edit the Bulletin. It had been initiated unofficially by him a few years back for the sake of aiding the exhibitors whose daily write-ups appeared therein, in addition to the outline of committee meetings, registrations, etc. On one occasion he had sought the Editor of the ANNALS OF INTERNAL MEDICINE to act as Editor of the Daily Bulletin, but the Editor had not found it possible to take on this added duty. Exhibitors had expressed the opinion that the Daily Bulletin was of little or no value to them, provided the Executive Offices would furnish them with lists of the registration at the end of the meeting. There had been very few comments of the members indicating appreciation of the Bulletin, and, therefore, because of the cost and tremendous amount of work connected with its daily appearance, it had been discontinued. Mr. Loveland, however, explained his willingness to place the matter before the Board of Regents and to continue its publication if so authorized.

Dr. Churchill, Governor for southern California, reported that he too had heard many remarks expressing disappointment about the discontinuance of the Daily Bulletin at the Detroit meeting. He said that he himself had missed it because being one who has some difficulty in associating names and faces, the Bulletin has been a great aid in identifying those present.

Dr. Cason, Governor for Florida, suggested that the College keep the situation in Havana, Cuba, open as a possibility for taking some of the men into the College membership. Some years ago the Board authorized him to keep the situation in mind, and he has continued his contacts, but conditions have been so chaotic that no steps have been taken.

Adjournment.

Attest: E. R. LOVELAND,
Executive Secretary